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A poetic understatement

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Sleep that satisfies *you*—you can count on an exceptionally wide margin of safety.^{7, 9} As always, caution patients about driving or drinking alcohol.



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nights of sleep...

DALMANE[®]

brand of
flurazepam HCl/Roche ©
sleep that satisfies

Please see adjacent page for references and summary of product information.



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TIMING IS KEY



MEDI-CAL CODE
5mg: 6355B
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EVERYTHING

Effective control time and time again¹

Effective control of fasting and postprandial glucose—patient after patient, meal after meal, year after year.

Insulin when it's needed

Insulin levels are rapidly elevated in response to a meal, then return promptly to basal levels after the meal challenge subsides.

Timed to minimize risks

Rapidly metabolized and excreted, with an excellent safety profile.¹ As with all sulfonylureas, hypoglycemia may occur.

In concert with diet in non-insulin-dependent diabetes mellitus



SYNCHRONIZED SULFONYLUREA THERAPY

Please see brief summary of Glucotrol® (glipizide) prescribing information on next page.

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New York, New York 10017

**Give your angina patients
what they're missing...**



CARDIZEM: FEW SIDE EFFECTS

diltiazem HCl/Marion

90^{mg} **NEW** **120**^{mg}
GREATER
DOSAGE
FLEXIBILITY

Antianginal action includes dilatation of coronary arteries, a decrease in vascular resistance/afterload, and a reduction in heart rate

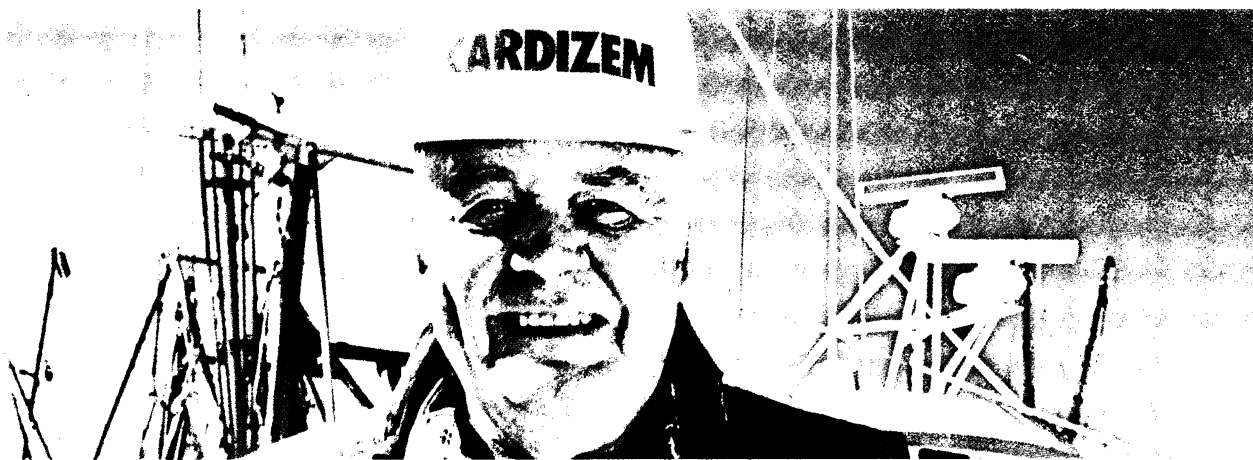
Proven efficacy when used alone in angina¹

Compatible with other antianginals^{2,3*}

A safe choice for angina patients with coexisting hypertension, asthma, COPD, or PVD^{4,5}

***See Warnings and Precautions.**

Please see brief summary of prescribing information on the next page.



CARDIZEM®

diltiazem HCl/Marion

FEW SIDE EFFECTS IN ANTIANGINAL THERAPY

60 mg tid or qid

Brief Summary

Professional Use Information

CARDIZEM®
(diltiazem HCl) 30 mg and 60 mg Tablets

CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

- Cardiac Conduction.** CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1,243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.
- Congestive Heart Failure.** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt). Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
- Hypotension.** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.
- Acute Hepatic Injury.** In rare instances, significant elevations in enzymes such as alkaline phosphatase, CPK, LDH, SGOT, SGPT, and other symptoms consistent with acute hepatic injury have been noted. These reactions have been reversible upon discontinuation of drug therapy. The relationship to CARDIZEM is uncertain in most cases, but probable in some. (See PRECAUTIONS.)

PRECAUTIONS

General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic

function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Drug Interaction. Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in *in vitro* bacterial tests. No intrinsic effect on fertility was observed in rats.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women, therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. Diltiazem is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If use of CARDIZEM is deemed essential, an alternative method of infant feeding should be instituted.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably asso-

ciated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences as well as their frequency of presentation are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%). In addition, the following events were reported infrequently (less than 1%):

Cardiovascular:	Angina, arrhythmia, AV block (first degree), AV block (second or third degree — see conduction warning), bradycardia, congestive heart failure, flushing, hypotension, palpitations, syncope.
Nervous System:	Amnesia, gait abnormality, hallucinations, insomnia, nervousness, paresthesia, personality change, somnolence, tinnitus, tremor.
Gastrointestinal:	Anorexia, constipation, diarrhea, dysgeusia, dyspepsia, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH (see hepatic warnings), vomiting, weight increase.
Dermatologic:	Petechiae, pruritus, photosensitivity, urticaria.
Other:	Amblyopia, dyspnea, epistaxis, eye irritation, hyperglycemia, nasal congestion, nocturia, osteoarthral pain, polyuria, sexual difficulties.

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: alopecia, gingival hyperplasia, erythema multiforme, and leukopenia. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established. Issued 7/86 See complete Professional Use Information before prescribing.

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Another patient benefit product from



For a Different
Kind of Calm



Introducing
BuSpar[®]
(buspirone HCl)

For Brief Summary, please see the last page of this advertisement.

Mead Johnson
Pharmaceuticals
Introduces

BuSpar[®] (buspirone HCl)

Tablets
5 mg and 10 mg

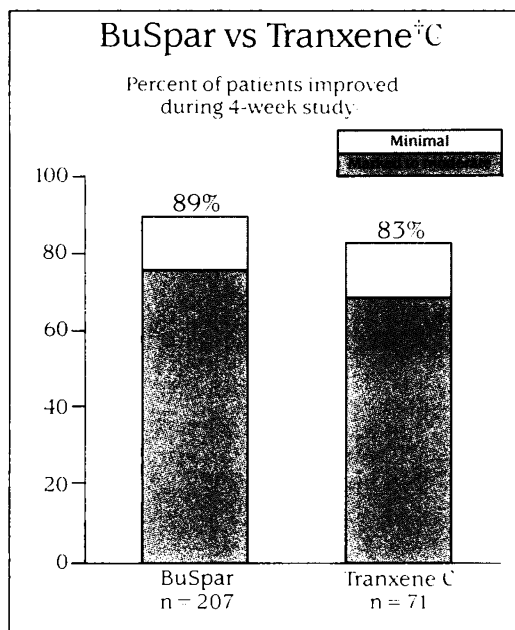
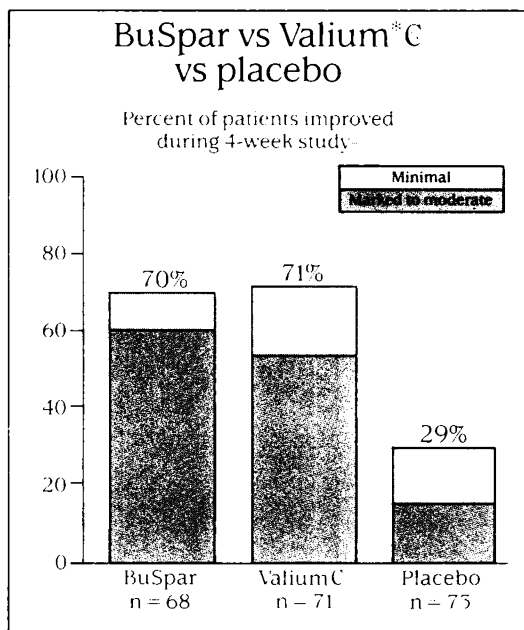
A different kind of calm

BuSpar—the first anxiolytic without CNS-depressant activity—has broken the connection between efficacy and unwanted sedative effects.

BuSpar gradually and comfortably provides relief of anxious symptoms—but produces no more drowsiness, motor impairment, or interaction with alcohol than does placebo.^{1,2,3}

Furthermore, in clinical studies, BuSpar exhibited no apparent abuse liability, and no withdrawal syndrome has been reported at the end of therapy.^{4,5}

Proven anxiolytic effectiveness over a 4-week course of therapy^{6,7}



*Registered trademark of Hoffmann-La Roche Inc for diazepam.

†Registered trademark of Abbott Pharmaceuticals, Inc for clorazepate.

‡Physician's assessment of global improvement.

Extensive clinical trials have shown that BuSpar produces impressive results over a four-week course of therapy. In comparative trials with Valium and Tranxene, 70% to 89% of patients receiving BuSpar were judged by their physicians to be improved at the end of therapy. Significant improvement was noted in a wide range of anxiety-related symptoms such as anxious mood, depressed mood,* and cardiovascular and gastrointestinal complaints.

*BuSpar is not indicated for the treatment of primary depressive disorder.

For Brief Summary, please see the last page of this advertisement.



BuSpar[®]

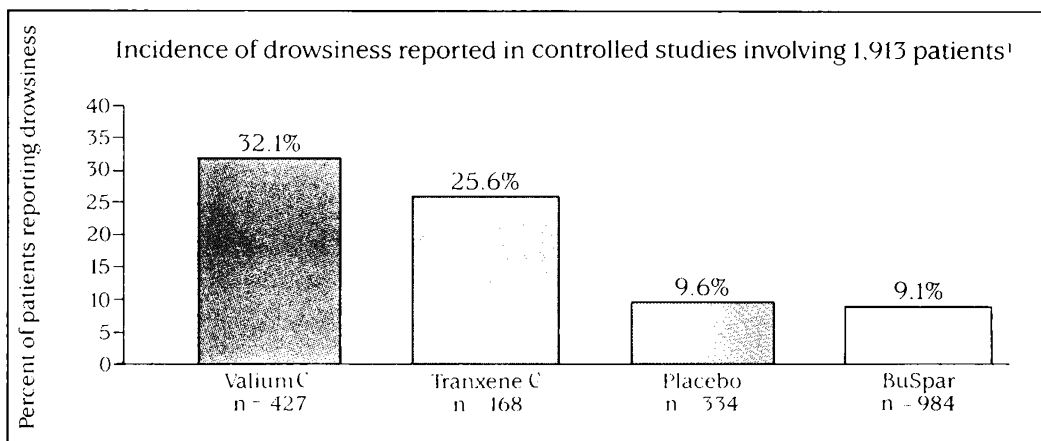
Tablets
5 mg and 10 mg

(buspirone HCl)

**Anxiolytic efficacy without
CNS-depressant activity**

**Incidence of drowsiness no greater
than placebo**

Because BuSpar does not replace symptoms with sedation, patients are alert and aware as well as anxiety-free during their waking hours.¹



**No impairment of
motor skills**

Controlled studies show that, unlike diazepam, BuSpar did not interfere with driving skills in normal subjects.²

NOTE: Patients should be cautioned about operating an automobile or using complex machinery until they are reasonably certain that BuSpar treatment does not affect them adversely.



No potentiation of the effects of alcohol

A controlled study in normal subjects showed that, unlike lorazepam, BuSpar did not augment the effects of alcohol.*³



No apparent abuse liability

Extensive preclinical information and clinical data from studies in two populations, recreational users of sedatives and alcohol-dependent patients, demonstrate that BuSpar does not have the characteristics of common substances of abuse. Therefore, BuSpar is not a controlled substance.^{4,8}

Well tolerated...with a low incidence of troublesome side effects

The most commonly observed adverse effects in controlled trials were dizziness (12%), nausea (8%), headache (6%), nervousness (5%), light-headedness (3%), and excitement (2%).

*While formal studies of the interaction of BuSpar with alcohol indicate that BuSpar does not increase alcohol-induced impairment in motor and mental performance, it is prudent to avoid concomitant use of alcohol and BuSpar.

For Brief Summary, please see the last page of this advertisement.



BuSpar[®] (buspirone HCl)

Tablets
5 mg and 10 mg

Subtle onset of effect

BuSpar relieves the symptoms of anxiety gradually and steadily. Generally, improvement will be noticeable within the first 7-10 days.

Prescribing recommendations

Initial dosage—5 mg t.i.d.

Week 1



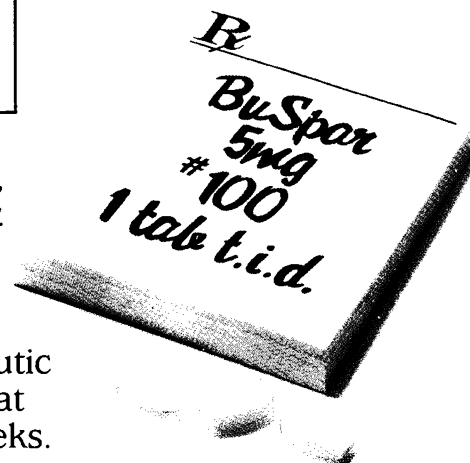
Dosage adjustment—5 mg/day increments, every 2-3 days, as needed, up to 60 mg/day.

Optimal daily dose—20-30 mg in divided doses, in most patients.

Length of therapy—To achieve full therapeutic benefit from BuSpar, it is recommended that treatment be prescribed for at least 3-4 weeks.

At the end of therapy

BuSpar therapy may be discontinued by simply stopping administration.



BuSpar is not a controlled substance.

Patient selection

BuSpar will not block the benzodiazepine withdrawal syndrome...therefore, the best candidates for BuSpar are those not currently taking benzodiazepines.

If you elect to switch a patient from a benzodiazepine to BuSpar:

1. Carefully and completely withdraw the patient from the benzodiazepine according to the benzodiazepine manufacturer's instructions before initiating BuSpar therapy.
2. Remember that benzodiazepine withdrawal symptoms, such as irritability, anxiety, agitation, insomnia, sweating, and sometimes even seizures, may occur over varying time periods after discontinuation.

BuSpar...the first choice in anxiolytic therapy when:

- ☒ Treatment requires regular dosing for more than a few days
- ☒ Patient functioning is key to safe and successful treatment
- ☒ The potential for drug habituation, dependence, abuse, or a withdrawal syndrome is a concern

For Brief Summary, please see following page.



BuSpar (buspirone HCl)



CONTRAINDICATIONS:
Hypersensitivity to buspirone.

WARNINGS:

The administration of BuSpar to a patient taking a monoamine oxidase inhibitor (MAOI) may pose a hazard. There have been reports of the occurrence of elevated blood pressure when BuSpar has been added to a regimen including an MAOI. Therefore, it is recommended that BuSpar not be used concomitantly with an MAOI.

Because BuSpar has no established antipsychotic activity, it should not be employed in lieu of appropriate antipsychotic treatment.

PRECAUTIONS:

General—

Interference with cognitive and motor performance:

Studies indicate that BuSpar is less sedating than other anxiolytics and that it does not produce significant functional impairment. However, its CNS effects in any individual patient may not be predictable. Therefore, patients should be cautioned about operating an automobile or using complex machinery until they are reasonably certain that buspirone treatment does not affect them adversely.

While formal studies of the interaction of BuSpar with alcohol indicate that buspirone does not increase alcohol-induced impairment in motor and mental performance, it is prudent to avoid concomitant use of alcohol and buspirone.

Potential for withdrawal reactions in sedative/hypnotic/anxiolytic drug-dependent patients:

Because BuSpar does not exhibit cross-tolerance with benzodiazepines and other common sedative/hypnotic drugs, it will not block the withdrawal syndrome often seen with cessation of therapy with these drugs. Therefore, before starting therapy with BuSpar, it is advisable to withdraw patients gradually, especially patients who have been using a CNS depressant drug chronically, from their prior treatment. Rebound or withdrawal symptoms may occur over varying time periods, depending in part on the type of drug, and its effective half-life of elimination.

The syndrome of withdrawal from sedative/hypnotic/anxiolytic drugs can appear as any combination of irritability, anxiety, agitation, insomnia, tremor, abdominal cramps, muscle cramps, vomiting, sweating, flu-like symptoms without fever, and occasionally, even as seizures.

Possible concerns related to buspirone's binding to dopamine receptors:

Because buspirone can bind to central dopamine receptors, a question has been raised about its potential to cause acute and chronic changes in dopamine mediated neurological function (e.g., dystonia, pseudoparkinsonism, akathisia, and tardive dyskinesia). Clinical experience in controlled trials has failed to identify any significant neuroleptic-like activity; however, a syndrome of restlessness, appearing shortly after initiation of treatment, has been reported in some small fraction of buspirone-treated patients. The syndrome may be explained in several ways. For example, buspirone may increase central noradrenergic activity; alternatively, the effect may be attributable to dopaminergic effects (i.e., represent akathisia). Obviously, the question cannot be totally resolved at this point in time. Generally, long-term sequelae of any drug's use can be identified only after several years of marketing.

Information for Patients:

Patients should be instructed to inform their physician about any medications, prescription or non-prescription, alcohol or drugs they are now taking or plan to take during treatment with buspirone; to inform their physician if they are pregnant, are planning to become pregnant, or become pregnant while taking buspirone; to inform their physician if they are breast feeding; and not to drive a car or operate potentially dangerous machinery until they experience how this medication affects them.

Drug Interactions:

Concomitant use with other CNS active drugs should be approached with caution. There is one report suggesting that the concomitant use of Desyrel® (trazodone) and BuSpar may have caused 3- to 6-fold elevations on SGPT (ALT) in a few patients. In a similar study, attempting to replicate this finding, no interactive effect on hepatic transaminases was identified. Buspirone does not displace tightly bound drugs like phenytoin, propranolol and warfarin from serum proteins, but may displace less firmly bound drugs like digoxin. (See WARNINGS)

Carcinogenesis, Mutagenesis, Impairment of Fertility:

No evidence of carcinogenic potential was observed in rats or mice; buspirone did not induce point mutations, nor was DNA damage observed; chromosomal aberrations or abnormalities did not occur.

Pregnancy:

Teratogenic Effects:

Pregnancy Category B: Should be used during pregnancy only if clearly needed.

Nursing Mothers:

Administration to nursing women should be avoided if clinically possible.

Pediatric Use:

The safety and effectiveness have not been determined in individuals below 18 years of age.

Use in the Elderly:

No unusual adverse age-related phenomena have been identified in elderly patients.

Use in Patients with Impaired Hepatic or Renal Function:

Since buspirone is metabolized by the liver and excreted by the kidneys, its administration to patients with severe hepatic or renal impairment cannot be recommended.

ADVERSE REACTIONS (See also Precautions):

Commonly Observed:

The more commonly observed untoward events associated with the use of BuSpar not seen at an equivalent incidence among placebo-treated patients include dizziness, nausea, headache, nervousness, light-headedness and excitement.

Associated with Discontinuation of Treatment:

The more common events causing discontinuation included central nervous system disturbances (3.4%)—primarily dizziness, insomnia, nervousness, drowsiness, and light-headed feeling; gastrointestinal disturbances (1.2%)—primarily nausea; and miscellaneous disturbances (1.1%)—primarily headache and fatigue. In addition, 3.4% of patients had multiple com-

plaints, none of which could be characterized as primary.

Incidence in Controlled Clinical Trials:

Adverse events that occurred at a frequency of 1% or more among 477 patients who received buspirone in four-week, controlled trials: **Cardiovascular:** tachycardia/palpitations 1%. **CNS:** dizziness 12%, drowsiness 10%, nervousness 5%, insomnia 3%, light-headedness 3%, decreased concentration 2%, excitement 2%, anger/hostility 2%, confusion 2%, depression 2%. **EENT:** blurred vision 2%. **Gastrointestinal:** nausea 8%, dry mouth 3%, abdominal/gastric distress 2%, diarrhea 2%, constipation 1%, vomiting 1%. **Musculoskeletal:** musculo-skeletal aches/pains 1%. **Neurological:** numbness 2%, paresthesia 1%, incoordination 1%, tremor 1%. **Skin:** skin rash 1%. **Miscellaneous:** headache 6%, fatigue 4%, weakness 2%, sweating/clamminess 1%.

Other Events Observed During the Entire Pre-Marketing Evaluation:

The following list includes all other adverse events reasonably associated with the use of buspirone in approximately 3000 subjects who took multiple doses of the drug under various conditions in well-controlled studies as well as open and uncontrolled clinical settings. The relative frequency of these adverse events is defined as follows: Frequent are those occurring in at least 1/100 patients; infrequent are those occurring in 1/100 to 1/1000 patients; and rare are those occurring in less than 1/1000 patients. **Cardiovascular:** Frequent was nonspecific chest pain; infrequent were syncope, hypotension and hypertension; rare were cerebrovascular accident, congestive heart failure, myocardial infarction, cardiomyopathy and bradycardia. **Central Nervous System:** Frequent were dream disturbances; infrequent were depersonalization, dysphoria, noise intolerance, euphoria, akathisia, fearfulness, loss of interest, disassociative reaction, hallucinations, suicidal ideation and seizures; rare were feelings of claustrophobia, cold intolerance, stupor, and slurred speech and psychosis. **EENT:** Frequent were tinnitus, sore throat and nasal congestion. Infrequent were redness and itching of the eyes, altered taste, altered smell, and conjunctivitis; rare were inner ear abnormality, eye pain, photophobia, and pressure on eyes. **Endocrine:** Rare were galactorrhea and thyroid abnormality. **Gastrointestinal:** Infrequent were flatulence, anorexia, increased appetite, salivation, irritable colon and rectal bleeding; rare was burning of the tongue. **Genitourinary:** Infrequent were urinary frequency, urinary hesitancy, menstrual irregularity and spotting, and dysuria; rare were amenorrhea, pelvic inflammatory disease, enuresis and nocturia. **Musculoskeletal:** Infrequent were muscle cramps, muscle spasms, rigid/stiff muscles, and arthralgias. **Neurological:** Infrequent were involuntary movements and slowed reaction time; rare was muscle weakness. **Respiratory:** Infrequent were hyperventilation, shortness of breath and chest congestion; rare was epistaxis. **Sexual Function:** Infrequent were decreased or increased libido; rare were delayed ejaculation and impotence. **Skin:** Infrequent were edema, pruritus, flushing, easy bruising, hair loss, dry skin, facial edema and blisters; rare were acne and thinning of nails. **Clinical Laboratory:** Infrequent were increases in hepatic aminotransferases (SGOT, SGPT); rare were eosinophilia, leukopenia and thrombocytopenia. **Miscellaneous:** Infrequent were weight gain, fever, roaring sensation in the head, weight loss and malaise; rare were alcohol abuse, bleeding disturbance, loss of voice and hiccoughs.

DRUG ABUSE AND DEPENDENCE:

Controlled Substance Class:

BuSpar is not a controlled substance.

Physical and Psychological Dependence:

Buspirone has shown no potential for abuse or diversion and there is no evidence that it causes tolerance, or either physical or psychological dependence. However, since it is difficult to predict from experiments the extent to which a CNS active drug will be misused, diverted and/or abused once marketed, physicians should carefully evaluate patients for a history of drug abuse and follow such patients closely, observing them for signs of buspirone misuse or abuse (e.g., development of tolerance, incrementation of dose, drug-seeking behavior).

OVERDOSAGE:

Signs and Symptoms:

No deaths have been reported in humans either with deliberate or accidental overdosage. At doses approaching 375 mg/day, the following symptoms were observed: nausea, vomiting, dizziness, drowsiness, miosis, and gastric distress.

Recommended Overdose Treatment:

General symptomatic and supportive measures should be used along with immediate gastric lavage. No specific antidote is known and dialyzability of buspirone has not been determined.

For complete details, see Prescribing Information or consult your Mead Johnson Pharmaceutical Division Representative.

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8. Griffith JD, et al: Investigation of the abuse liability of buspirone in alcohol-dependent patients. *Amer J Med* 1986;80 (3B):30-35.

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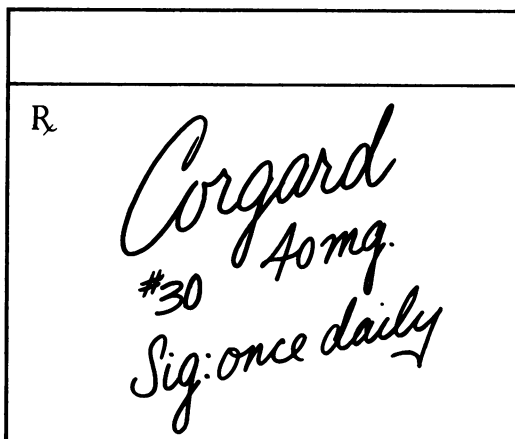
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for the hypertensive patient*



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Nadolol Tablets USP

DESCRIPTION: CORGARD (nadolol) is a synthetic nonselective beta-adrenergic receptor blocking agent.

CONTRAINDICATIONS: Bronchial asthma, sinus bradycardia and greater than first degree conduction block, cardiogenic shock, and overt cardiac failure (see WARNINGS).

WARNINGS: Cardiac Failure—Sympathetic stimulation may be a vital component supporting circulatory function in congestive heart failure, and its inhibition by beta-blockade may precipitate more severe failure. Although beta-blockers should be avoided in overt congestive heart failure, if necessary, they can be used with caution in patients with a history of failure who are well-compensated, usually with digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle. IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta-blockers can, in some cases, lead to cardiac failure; therefore, at first sign or symptom of heart failure, digitalize and/or give diuretics, and closely observe response, or discontinue nadolol (gradually if possible).

Exacerbation of Ischemic Heart Disease Following Abrupt Withdrawal—

Hypersensitivity to catecholamines has been observed in patients withdrawn from beta-blocker therapy; exacerbation of angina and, in some cases, myocardial infarction have occurred after abrupt discontinuation of such therapy. When discontinuing chronic use of nadolol, particularly in patients with ischemic heart disease, gradually reduce dosage over a 1- to 2-week period and carefully monitor the patient. Reinstitution nadolol promptly (at least temporarily) and take other measures appropriate for management of unstable angina if angina markedly worsens or acute coronary insufficiency develops. Warn patients not to interrupt or discontinue therapy without physician's advice. Because coronary artery disease is common and may be unrecognized, it may be prudent not to discontinue nadolol therapy abruptly even in patients treated only for hypertension.

Nonallergic Bronchospasm (e.g., chronic bronchitis, emphysema)—PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA-BLOCKERS. Administer nadolol with caution since it may block bronchodilation produced by endogenous or exogenous catecholamine stimulation of beta₂ receptors.

Major Surgery—Because beta blockade impairs the ability of the heart to respond to reflex stimuli and may increase risks of general anesthesia and surgical procedures, resulting in protracted hypotension or low cardiac output, it has generally been suggested that such therapy should be withdrawn several days prior to surgery. Recognition of the increased sensitivity to catecholamines of patients recently withdrawn from beta-blocker therapy, however, has made this recommendation controversial. If possible, withdraw beta-blockers well before surgery takes place. In emergency surgery, inform the anesthesiologist that the patient is on beta-blocker therapy. Use of beta-receptor agonists such as isoproterenol, dopamine, dobutamine, or levaterenol can reverse the effects of nadolol. Difficulty in restarting and maintaining the heart beat has also been reported with beta-adrenergic receptor blocking agents.

Diabetes and Hypoglycemia—Beta-adrenergic blockade may prevent the appearance of premonitory signs and symptoms (e.g., tachycardia and blood pressure changes) of acute hypoglycemia. This is especially important with labile diabetics. Beta-blockade also reduces release of insulin in response to hyperglycemia; therefore, it may be necessary to adjust dose of antidiabetic drugs.

Thyrotoxicosis—Beta-adrenergic blockade may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. To avoid abrupt withdrawal of beta-adrenergic blockade which might precipitate a thyroid storm, carefully manage patients suspected of developing thyrotoxicosis.

PRECAUTIONS: Impaired Renal Function—Use nadolol with caution (see DOSAGE AND ADMINISTRATION section of package insert).

Information for Patients—Warn patients, especially those with evidence of coronary artery insufficiency, against interruption or discontinuation of nadolol without physician's advice. Although cardiac failure rarely occurs in properly selected patients, advise patients being treated with beta-adrenergic blocking agents to consult physician at first sign of impending failure. Advise patients in event of missed doses.

Drug Interactions—Concurrent administration may result in interactions with: Anesthetics, general—exaggeration of the hypotension induced by general anesthetics (see WARNINGS, Major Surgery). Antidiabetic drugs (oral agents and insulin)—hypoglycemia or hyperglycemia; adjust antidiabetic drug dosage accordingly (see WARNINGS, Diabetes and Hypoglycemia). Catecholamine-depleting drugs (e.g., reserpine)—additive effect; monitor closely for hypotension and/or excessive bradycardia.

Carcinogenesis, Mutagenesis, Impairment of Fertility—In 1 to 2 year oral toxicologic studies in mice, rats, and dogs, nadolol did not produce significant toxic effects. In 2-year oral carcinogenic studies in rats and mice, nadolol did not produce neoplastic, preneoplastic, or nonneoplastic pathologic lesions.

Pregnancy Category C—In animal reproduction studies with nadolol, evidence of embryo- and fetotoxicity was found in rabbits (but not in rats or hamsters) at doses 5 to 10 times greater (on a mg/kg basis) than maximum indicated human dose; no teratogenic potential was seen in any of these species. There are no well-controlled studies in pregnant women; therefore, use nadolol in pregnant women only if potential benefit justifies potential risk to the fetus. Neonates of mothers who received nadolol at parturition have exhibited bradycardia, hypoglycemia and associated symptoms.

Nursing Mothers—Nadolol is excreted in human milk. Exercise caution when nadolol is administered to a nursing woman.

Pediatric Use—Safety and effectiveness in children have not been established.

ADVERSE REACTIONS: Most adverse effects have been mild and transient and have rarely required nadolol withdrawal.

Cardiovascular—Bradycardia with heart rates of less than 60 beats per minute occurs commonly, and heart rates below 40 beats per minute and/or symptomatic bradycardia were seen in about 2 of 100 patients. Symptoms of peripheral vascular insufficiency, usually of the Raynaud type, have occurred in approximately 2 of 100 patients. Cardiac failure, hypotension, and rhythm/conduction disturbances have each occurred in about 1 of 100 patients. Single instances of first degree and third degree heart block have been reported; intensification of AV block is a known effect of beta-blockers (see also CONTRAINDICATIONS, WARNINGS, and PRECAUTIONS). **Central Nervous System**—Dizziness or fatigue reported in approximately 2 of 100 patients; paresthesias, sedation, and change in behavior reported in approximately 6 of 1000 patients. **Respiratory**—Bronchospasm reported in approximately 1 of 1000 patients (see CONTRAINDICATIONS and WARNINGS). **Gastrointestinal**—Nausea, diarrhea, abdominal discomfort, constipation, vomiting, indigestion, anorexia, bloating, and flatulence each reported in 1 to 5 of 1000 patients. **Miscellaneous**—Each of the following reported in 1 to 5 of 1000 patients: rash; pruritus; headache; dry mouth, eyes, or skin; impotence or decreased libido; facial swelling; weight gain; slurred speech; cough; nasal stuffiness; sweating; tinnitus; blurred vision; infrequent reversible alopecia.

The following adverse reactions have been reported in patients taking nadolol and/or other beta-adrenergic blocking agents, but no causal relationship to nadolol has been established.

Central Nervous System—reversible mental depression progressing to cataplexy; visual disturbances; hallucinations; an acute reversible syndrome characterized by disorientation for time and place; short-term memory loss, emotional lability with slightly clouded sensorium; decreased performance on neuropsychometrics. **Gastrointestinal**—mesenteric arterial thrombosis; ischemic colitis; elevated liver enzymes. **Hematologic**—agranulocytosis; thrombocytopenia or nonthrombocytopenic purpura. **Allergic**—fever combined with aching and sore throat; laryngospasm; respiratory distress. **Miscellaneous**—pemphigoid rash; hypertensive reaction in patients with pheochromocytoma; sleep disturbances; Peyronie's disease. The oculomucocutaneous syndrome associated with prazosin has not been reported with nadolol.

OVERDOSAGE: Nadolol can be removed from the general circulation by hemodialysis. In addition to gastric lavage, employ the following measures as appropriate. In determining duration of corrective therapy, take note of long duration of effect of nadolol.

Excessive Bradycardia—Administer atropine (0.25 to 1.0 mg). If there is no response to vagal blockade, administer isoproterenol cautiously.

Cardiac Failure—Administer a digitalis glycoside and diuretic. It has been reported that glucagon may also be useful in this situation.

Hypotension—Administer vasopressors, e.g., epinephrine or levaterenol. (There is evidence that epinephrine may be the drug of choice.)

Bronchospasm—Administer a beta₂-stimulating agent and/or a theophylline derivative.

DOSAGE—For all patients, DOSAGE MUST BE INDIVIDUALIZED.

For **angina pectoris**, usual initial dose is 40 mg qd; may be gradually increased in 40 to 80 mg increments at 3 to 7 day intervals until optimum clinical response or pronounced slowing of the heart rate; usual maintenance dose is 40 or 80 mg qd (doses up to 160 or 240 mg daily may be needed). If treatment is to be discontinued, reduce dosage gradually over a period of 1 to 2 weeks (see WARNINGS).

For **hypertension**, usual initial dose is 40 mg qd; gradually increase in 40 to 80 mg increments until optimum blood pressure reduction is achieved; usual maintenance dose is 40 or 80 mg qd (doses up to 240 or 320 mg daily may be needed).

Patients with renal failure require adjustment in dosing interval; see package insert for dosage in these patients.


For full prescribing information consult package insert.

HOW SUPPLIED: In scored tablets containing 20, 40, 80, 120, or 160 mg nadolol per tablet in bottles of 100. The 40 mg, 80 mg, and 120 mg tablets are available in bottles of 1000 tablets. The 20 mg, 40 mg, and 80 mg tablets are also available in Unimatic® unit-dose packs of 100 tablets. (J4-156)



Advantages beyond control in hypertension

- *Good CNS side effect profile*
- *Preservation of renal blood flow*
- *Once-a-day convenience*



*Now
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20 mg
tablets*

CORGARD[®]
(nadolol tablets)

Advantages beyond control

Please see brief summary of prescribing information on adjacent page.

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First-step cardiovascular protection



Reduces workload of the heart by
reducing myocardial O_2 demand

Preserves K^+ balance

Normalizes stress-induced systolic
peaks with cardioselective
beta-one blockade

Contraindicated in sinus bradycardia, heart block
greater than first degree, cardiogenic shock, and
overt cardiac failure.

Please consult Brief Summary of Prescribing
Information on the following page.

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BRIEF SUMMARY (FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE INSERT)

CONTRAINDICATIONS

Hypertension and Angina

Lopressor is contraindicated in sinus bradycardia, heart block greater than first degree, cardiogenic shock, and overt cardiac failure (see **WARNINGS**).

Myocardial Infarction

Lopressor is contraindicated in patients with a heart rate < 45 beats/min; second- and third-degree heart block; significant first-degree heart block (P-R interval \geq 0.24 sec); systolic blood pressure < 100 mmHg; or moderate-to-severe cardiac failure (see **WARNINGS**).

WARNINGS

Hypertension and Angina

Cardiac Failure: Sympathetic stimulation is a vital component supporting circulatory function in congestive heart failure, and beta blockade carries the potential hazard of further depressing myocardial contractility and precipitating more severe failure. In hypertensive and angina patients who have congestive heart failure controlled by digitalis and diuretics, Lopressor should be administered cautiously. Both digitalis and Lopressor slow AV conduction.

In Patients Without a History of Cardiac Failure: Continued depression of the myocardium with beta-blocking agents over a period of time can, in some cases, lead to cardiac failure. At the first sign or symptom of impending cardiac failure, patients should be fully digitalized and/or given a diuretic. The response should be observed closely. If cardiac failure continues, despite adequate digitalization and diuretic therapy, Lopressor should be withdrawn.

Ischemic Heart Disease: Following abrupt cessation of therapy with certain beta-blocking agents, exacerbations of angina pectoris and, in some cases, myocardial infarction have occurred. When discontinuing chronically administered Lopressor, particularly in patients with ischemic heart disease, the dosage should be gradually reduced over a period of 1-2 weeks and the patient should be carefully monitored. If angina markedly worsens or acute coronary insufficiency develops, Lopressor administration should be reinstated promptly, at least temporarily, and other measures appropriate for the management of unstable angina should be taken. Patients should be warned against interruption or discontinuation of therapy without the physician's advice. Because coronary artery disease is common and may be unrecognized, it may be prudent not to discontinue Lopressor therapy abruptly even in patients treated only for hypertension.

Bronchospastic Diseases: PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD, IN GENERAL, NOT RECEIVE BETA BLOCKERS. Because of its relative beta₂ selectivity, however, Lopressor may be used with caution in patients with bronchospastic disease who do not respond to, or cannot tolerate, other antihypertensive treatment. Since beta₂ selectivity is not absolute, a beta₂-stimulating agent should be administered concomitantly, and the lowest possible dose of Lopressor should be used. In these circumstances it would be prudent initially to administer Lopressor in smaller doses three times daily, instead of larger doses two times daily, to avoid the higher plasma levels associated with the longer dosing interval. (See **DOSAGE AND ADMINISTRATION**.)

Major Surgery: The necessity or desirability of withdrawing beta-blocking therapy prior to major surgery is controversial; the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

Lopressor, like other beta blockers, is a competitive inhibitor of beta-receptor agonists, and its effects can be reversed by administration of such agents, e.g., dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in restarting and maintaining the heart beat has also been reported with beta blockers.

Diabetes and Hypoglycemia: Lopressor should be used with caution in diabetic patients if a beta-blocking agent is required. Beta blockers may mask tachycardia occurring with hypoglycemia, but other manifestations such as dizziness and sweating may not be significantly affected.

Thyrotoxicosis: Beta-adrenergic blockade may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. Patients suspected of developing thyrotoxicosis should be managed carefully to avoid abrupt withdrawal of beta blockade, which might precipitate a thyroid storm.

Myocardial Infarction

Cardiac Failure: Sympathetic stimulation is a vital component supporting circulatory function, and beta blockade carries the potential hazard of depressing myocardial contractility and precipitating or exacerbating minimal cardiac failure.

During treatment with Lopressor, the hemodynamic status of the patient should be carefully monitored. If heart failure occurs or persists despite appropriate treatment, Lopressor should be discontinued.

Bradycardia: Lopressor produces a decrease in sinus heart rate in most patients; this decrease is greatest among patients with high initial heart rates and least among patients with low initial heart rates. Acute myocardial infarction (particularly inferior infarction) may in itself produce significant lowering of the sinus rate. If the sinus rate decreases to < 40 beats/min, particularly if associated with evidence of lowered cardiac out-

put, atropine (0.25-0.5 mg) should be administered intravenously. If treatment with atropine is not successful, Lopressor should be discontinued, and cautious administration of isoproterenol or installation of a cardiac pacemaker should be considered.

AV Block: Lopressor slows AV conduction and may produce significant first- (P-R interval \geq 0.26 sec), second-, or third-degree heart block. Acute myocardial infarction also produces heart block.

If heart block occurs, Lopressor should be discontinued and atropine (0.25-0.5 mg) should be administered intravenously. If treatment with atropine is not successful, cautious administration of isoproterenol or installation of a cardiac pacemaker should be considered.

Hypotension: If hypotension (systolic blood pressure \leq 90 mmHg) occurs, Lopressor should be discontinued, and the hemodynamic status of the patient and the extent of myocardial damage carefully assessed. Invasive monitoring of central venous, pulmonary capillary wedge, and arterial pressures may be required. Appropriate therapy with fluids, positive inotropic agents, balloon counterpulsation, or other treatment modalities should be instituted. If hypotension is associated with sinus bradycardia or AV block, treatment should be directed at reversing these (see above).

Bronchospastic Diseases: PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD, IN GENERAL, NOT RECEIVE BETA BLOCKERS. Because of its relative beta₂ selectivity, Lopressor may be used with extreme caution in patients with bronchospastic disease. Because it is unknown to what extent beta₂-stimulating agents may exacerbate myocardial ischemia and the extent of infarction, these agents should not be used prophylactically. If bronchospasm not related to congestive heart failure occurs, Lopressor should be discontinued. A theophylline derivative or a beta₂ agonist may be administered cautiously, depending on the clinical condition of the patient. Both theophylline derivatives and beta₂ agonists may produce serious cardiac arrhythmias.

PRECAUTIONS

General

Lopressor should be used with caution in patients with impaired hepatic function.

Information for Patients

Patients should be advised to take Lopressor regularly and continuously, as directed, with or immediately following meals. If a dose should be missed, the patient should take only the next scheduled dose (without doubling it). Patients should not discontinue Lopressor without consulting the physician.

Patients should be advised (1) to avoid operating automobiles and machinery or engaging in other tasks requiring alertness until the patient's response to therapy with Lopressor has been determined; (2) to contact the physician if any difficulty in breathing occurs; (3) to inform the physician or dentist before any type of surgery that he or she is taking Lopressor.

Laboratory Tests

Clinical laboratory findings may include elevated levels of serum transaminase, alkaline phosphatase, and lactate dehydrogenase.

Drug Interactions

Catecholamine-depleting drugs (e.g., reserpine) may have an additive effect when given with beta-blocking agents. Patients treated with Lopressor plus a catecholamine depletor should therefore be closely observed for evidence of hypotension or marked bradycardia, which may produce vertigo, syncope, or postural hypotension.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals have been conducted to evaluate carcinogenic potential. In 2-year studies in rats at three oral dosage levels of up to 800 mg/kg per day, there was no increase in the development of spontaneously occurring benign or malignant neoplasms of any type. The only histologic changes that appeared to be drug related were an increased incidence of generally mild focal accumulation of foamy macrophages in pulmonary alveoli and a slight increase in biliary hyperplasia. Neither finding represents symptoms of a known disease entity in man. In a 21-month study in Swiss albino mice at three oral dosage levels of up to 750 mg/kg per day, benign lung tumors (small adenomas) occurred more frequently in female mice receiving the highest dose than in untreated control animals. There was no increase in malignant or total (benign plus malignant) lung tumors, nor in the overall incidence of tumors or malignant tumors. This 21-month study was repeated in CD-1 mice, and no statistically or biologically significant differences were observed between treated and control mice of either sex for any type of tumor.

All mutagenicity tests performed (a dominant lethal study in mice, chromosome studies in somatic cells, a Salmonella/mammalian-microsome mutagenicity test, and a nucleus anomaly test in somatic interphase nuclei) were negative.

No evidence of impaired fertility due to Lopressor was observed in a study performed in rats at doses up to 55.5 times the maximum daily human dose of 450 mg.

Pregnancy Category C

Lopressor has been shown to increase postimplantation loss and decrease neonatal survival in rats at doses up to 55.5 times the maximum daily human dose of 450 mg. Distribution studies in mice confirm exposure of the fetus when Lopressor is administered to the pregnant animal. These studies have revealed no evidence of impaired fertility or teratogenicity. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers

Lopressor is excreted in breast milk in very small quantity. An infant consuming 1 liter of breast milk daily would receive a dose of less than 1 mg of the drug. Caution should be exercised when Lopressor is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Hypertension and Angina

Most adverse effects have been mild and transient.

Central Nervous System: Tiredness and dizziness have occurred in about 10 of 100 patients. Depression has been reported in about 5 of 100 patients. Mental confusion and short-term memory loss have been reported. Headache, nightmares, and insomnia have also been reported.

Cardiovascular: Shortness of breath and bradycardia have occurred in approximately 3 of 100 patients. Cold extremities; arterial insufficiency, usually of the Raynaud type; palpitations; congestive heart failure; peripheral edema; and hypotension have been reported in about 1 of 100 patients. (See **CONTRAINDICATIONS, WARNINGS, and PRECAUTIONS**.)

Respiratory: Wheezing (bronchospasm) and dyspnea have been reported in about 1 of 100 patients (see **WARNINGS**).

Gastrointestinal: Diarrhea has occurred in about 5 of 100 patients. Nausea, dry mouth, gastric pain, constipation, flatulence, and heartburn have been reported in about 1 of 100 patients.

Hypersensitive Reactions: Pruritus or rash have occurred in about 5 of 100 patients. Worsening of psoriasis has also been reported.

Miscellaneous: Peyronie's disease has been reported in fewer than 1 of 100,000 patients. Musculoskeletal pain, blurred vision, and tinnitus have also been reported.

There have been rare reports of reversible alopecia, agranulocytosis, and dry eyes. Discontinuation of the drug should be considered if any such reaction is not otherwise explicable.

The oculomucocutaneous syndrome associated with the beta blocker practolol has not been reported with Lopressor.

Myocardial Infarction

Central Nervous System: Tiredness has been reported in about 1 of 100 patients. Vertigo, sleep disturbances, hallucinations, headache, dizziness, visual disturbances, confusion, and reduced libido have also been reported, but a drug relationship is not clear.

Cardiovascular: In the randomized comparison of Lopressor and placebo described in the **CLINICAL PHARMACOLOGY** section, the following adverse reactions were reported:

	Lopressor	Placebo
Hypotension (systolic BP < 90 mmHg)	27.4%	23.2%
Bradycardia (heart rate < 40 beats/min)	15.9%	6.7%
Second- or third-degree heart block	4.7%	4.7%
First-degree heart block (P-R \geq 0.26 sec)	5.3%	1.9%
Heart failure	27.5%	29.6%

Respiratory: Dyspnea of pulmonary origin has been reported in fewer than 1 of 100 patients.

Gastrointestinal: Nausea and abdominal pain have been reported in fewer than 1 of 100 patients.

Dermatologic: Rash and worsened psoriasis have been reported, but a drug relationship is not clear.

Miscellaneous: Unstable diabetes and claudication have been reported, but a drug relationship is not clear.

Potential Adverse Reactions

A variety of adverse reactions not listed above have been reported with other beta-adrenergic blocking agents and should be considered potential adverse reactions to Lopressor.

Central Nervous System: Reversible mental depression progressing to cataplexy; an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics.

Cardiovascular: Intensification of AV block (see **CONTRAINDICATIONS**).

Hematologic: Agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

Hypersensitive Reactions: Fever combined with aching and sore throat, laryngospasm, and respiratory distress.

OVERDOSAGE

Acute Toxicity

Several cases of overdosage have been reported, some leading to death.

Oral LD₅₀'s (mg/kg): mice, 1158-2460; rats, 3090-4670.

Signs and Symptoms

Potential signs and symptoms associated with overdosage with Lopressor are bradycardia, hypotension, bronchospasm, and cardiac failure.

Treatment

There is no specific antidote.

In general, patients with acute or recent myocardial infarction may be more hemodynamically unstable than other patients and should be treated accordingly (see **WARNINGS, Myocardial Infarction**).

On the basis of the pharmacologic actions of Lopressor, the following general measures should be employed:

Elimination of the Drug: Gastric lavage should be performed.

Bradycardia: Atropine should be administered. If there is no response to vagal blockade, isoproterenol should be administered cautiously.

Hypotension: A vasopressor should be administered, e.g., levaterenol or dopamine.

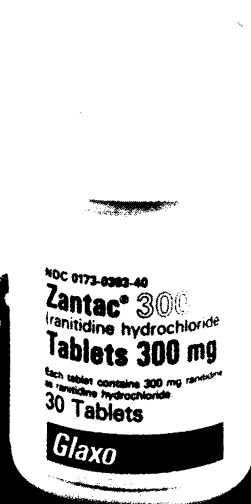
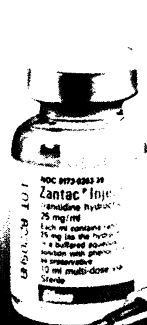
Bronchospasm: A beta₂-stimulating agent and/or a theophylline derivative should be administered.

Cardiac Failure: A digitalis glycoside and diuretic should be administered. In shock resulting from inadequate cardiac contractility, administration of dobutamine, isoproterenol, or glucagon may be considered.

Geigy

Geigy Pharmaceuticals
Division of CIBA-Geigy Corporation
Ardley, New York 10502

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has rapidly emerged as a
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2 ml, 10 ml vials (50 mg/2 ml)

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Physicians Practice Management
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Software for the M.D.

The portrait of anxiety



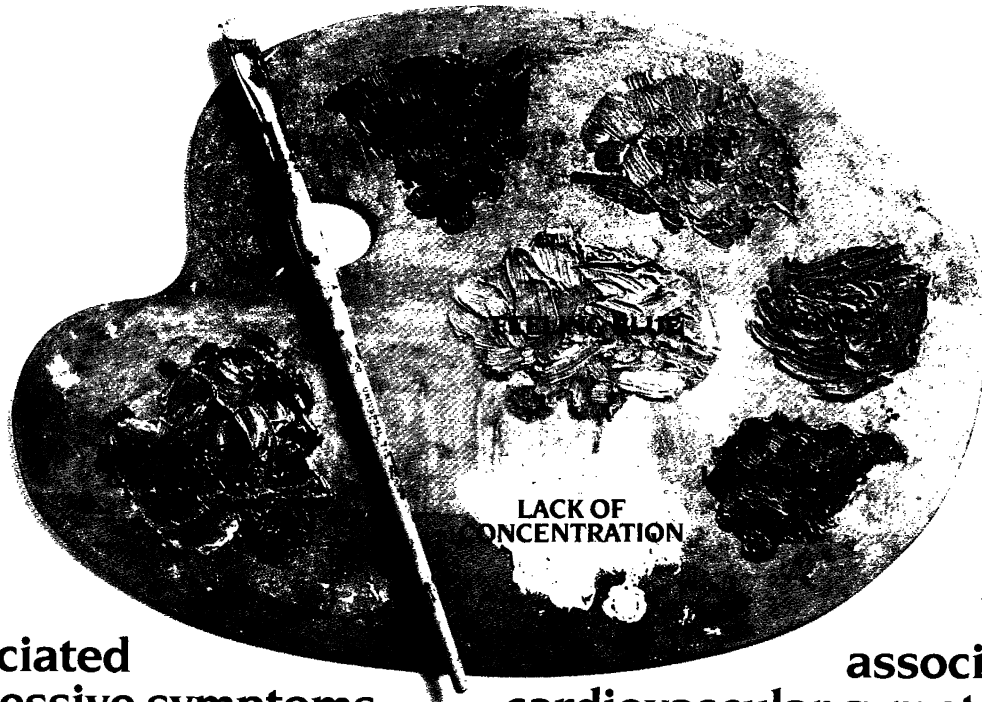
Upjohn

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Kalamazoo, Michigan 49001 USA

Please see adjacent page for brief summary of prescribing information.

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is often complicated



With associated depressive symptoms.

In double-blind, four-week clinical trials in 632 patients with moderate to severe anxiety, therapy with XANAX was compared with placebo.

XANAX was significantly more effective ($P < .001$) than placebo in relieving the anxiety, with over half of the patients showing marked to moderate improvement by the first evaluation period (one week).

In addition, over 70% of these patients experienced associated moderate to severe depressed mood. XANAX was shown to be significantly more effective ($P < .014$) than placebo in improving the associated depressed mood.



With associated cardiovascular symptoms.

Almost 60% of patients in the study had anxiety with associated cardiovascular symptoms even though cardiovascular disease had been ruled out. XANAX was shown to effectively relieve anxiety including the associated cardiovascular symptoms.

XANAX, the first of a unique class—the triazolobenzodiazepines.

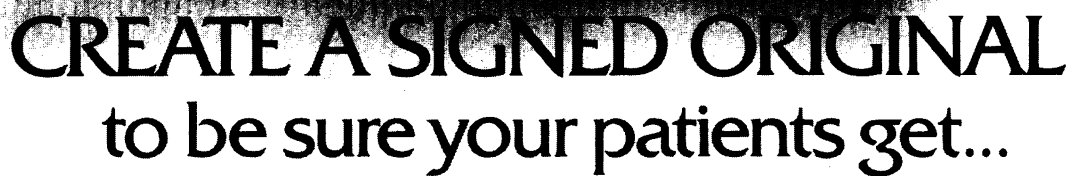
■ **Well tolerated**—Side effects, if they occur are generally observed at the beginning of therapy and usually disappear with continued medication. Drowsiness and light-headedness were the most commonly reported adverse reactions.

■ **Sustained efficacy**—No reported increase in dosage during 16-week clinical study, once an appropriate dosage was achieved. Since long-term effectiveness of XANAX has not been established, it is recommended that it not be used for longer than 16 weeks.

■ **Simple dosage**—0.25 to 0.5 mg t.i.d.

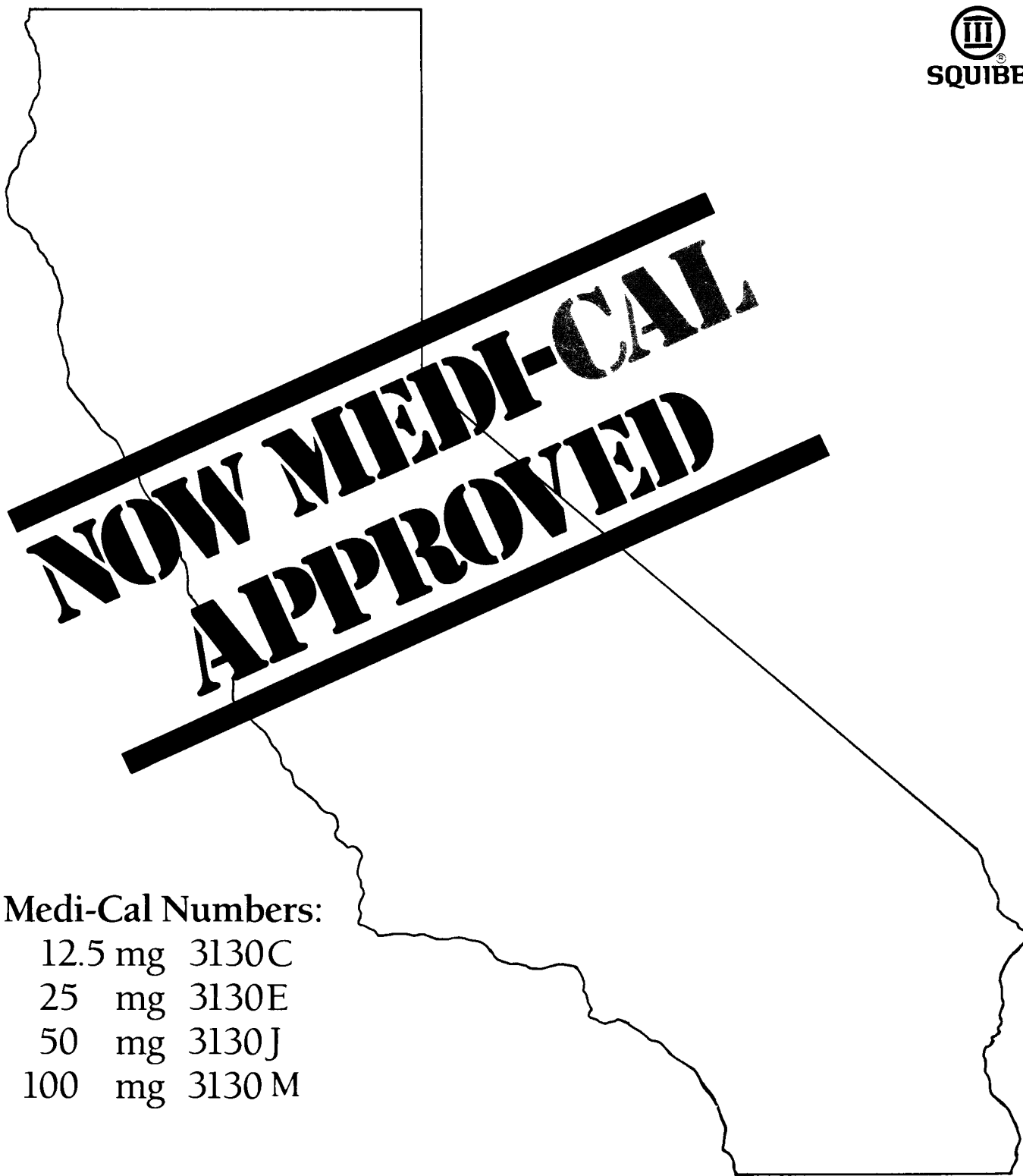


for the relief of complicated anxiety



Tablets: Contain Codeine Phosphate*: No. 3—30 mg;
No. 4—60 mg—plus Acetaminophen 300 mg.
Elixir: Each 5 mL contains 12 mg Codeine Phosphate* plus
120 mg Acetaminophen (Alcohol 7%).

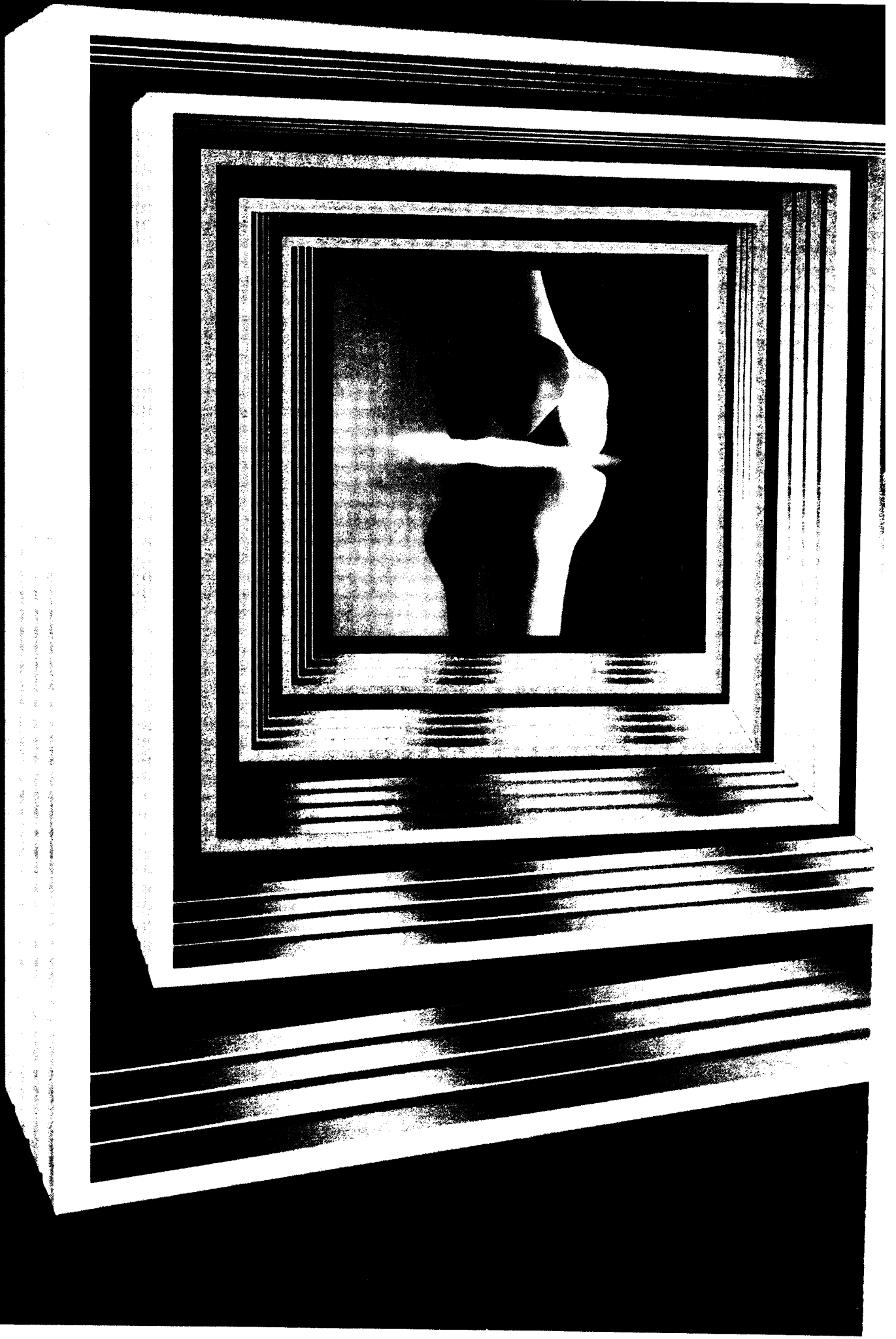
***Warning: May be habit forming.**



Medi-Cal Numbers:

12.5 mg	3130C
25 mg	3130E
50 mg	3130J
100 mg	3130M

CAUTION



Osteoarthritis and the Anti-inflammatory Threshold of Motrin

Inflammation is usually a factor in the pain of osteoarthritis. There's ample evidence of this,^{1,5} and it may explain why some patients require higher, anti-inflammatory doses of MOTRIN Tablets (ibuprofen).

Studies and experience have shown that at dosages up to 1200 mg/day, ibuprofen is primarily analgesic. Anti-inflammatory activity is added to effective analgesia in patients taking higher dosages of MOTRIN.⁶⁻⁸

MOTRIN 800 mg tablets: An easier way to reach the anti-inflammatory range

Extra-strength MOTRIN 800 mg tablets are a more convenient way to provide the higher doses required to maintain anti-inflammatory activity.

Just one 800 mg tablet t.i.d. provides 2400 mg/day for osteoarthritis patients who require higher doses of MOTRIN. If necessary, patients can take one tablet q.i.d. Doses above 3200 mg/day are not recommended. The lowest effective dosage should be used. Gastrosopic studies at varying doses show an increased tendency toward gastric irritation at higher doses. However, at comparable doses, gastric irritation is approximately half that seen with aspirin.

Please turn the page for references and a brief summary of prescribing information.

A stronger reason to prescribe MOTRIN in osteoarthritis

Motrin[®] 800mg TABLETS
ibuprofen

For the inflammation and the pain of osteoarthritis

Motrin[®] 800mg TABLETS

ibuprofen

A stronger reason to prescribe MOTRIN.

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MOTRIN[®] Tablets

(ibuprofen)

CONTRAINDICATIONS: Anaphylactoid reactions have occurred in individuals hypersensitive to MOTRIN or with the syndrome of nasal polyps, angioedema and bronchospastic reactivity to aspirin or other nonsteroidal anti-inflammatory agents.

WARNINGS: Peptic ulceration and G.I. bleeding, sometimes severe, have been reported. Ulceration, perforation and bleeding may end fatally. An association has not been established. Use MOTRIN under close supervision in patients with a history of upper gastrointestinal tract disease, after consulting ADVERSE REACTIONS. In patients with active peptic ulcer and active rheumatoid arthritis, try nonulcerogenic drugs, such as gold. If MOTRIN is used, observe the patient closely for signs of ulcer perforation or G.I. bleeding.

PRECAUTIONS: Blurred and/or diminished vision, scotomata, and/or changes in color vision have been reported. If these develop, discontinue MOTRIN and the patient should have an ophthalmologic examination, including central visual fields and color vision testing.

Fluid retention and edema have been associated with MOTRIN; use with caution in patients with a history of cardiac decompensation or hypertension.

MOTRIN can inhibit platelet aggregation and prolong bleeding time. Use with caution in persons with intrinsic coagulation defects and on anticoagulant therapy.

Patients should report signs or symptoms of gastrointestinal ulceration or bleeding, blurred vision, skin rash, weight gain, or edema.

Patients on prolonged corticosteroid therapy should have therapy tapered slowly when MOTRIN is added. The antipyretic, anti-inflammatory activity of MOTRIN may mask inflammation and fever.

As with other nonsteroidal anti-inflammatory drugs, borderline elevations of liver tests may occur in up to 15% of patients. These abnormalities may progress, may remain essentially unchanged, or may be transient with continued therapy. Meaningful elevations of SGPT or SGOT (AST) occurred in controlled clinical trials in less than 1% of patients. Severe hepatic reactions, including jaundice and cases of fatal hepatitis, have been reported with ibuprofen as with other nonsteroidal anti-inflammatory drugs. If liver disease develops or if systemic manifestations occur (e.g. eosinophilia, rash, etc.), MOTRIN should be discontinued.

In cross-study comparisons with 1200 mg to 3200 mg daily for several weeks, a slight dose-response decrease in hemoglobin/hematocrit was noted. The total decrease in hemoglobin usually does not exceed 1 gram.

Renal Effects: Long term administration of ibuprofen and other NSAID's to animals has resulted in renal papillary necrosis and other abnormal renal pathology. In humans, there have been reports of acute interstitial nephritis with hematuria, proteinuria, and occasionally nephrotic syndrome. In patients with prerenal conditions and reduced renal blood flow or blood volume, NSAID's may precipitate overt renal decompensation. Patients with impaired renal function, heart failure, liver dysfunction, those taking diuretics and the elderly are at greatest risk. Discontinuation of NSAID therapy is typically followed by recovery to the pretreatment state. In patients with renal impairment, reduced dosage may be necessary. Prospective studies of MOTRIN safety in patients with chronic renal failure have not been done.

Drug Interactions: Aspirin: Used concomitantly may decrease MOTRIN blood levels.

Coumarin: Bleeding has been reported in patients taking MOTRIN and coumarin.

Pregnancy and nursing mothers: MOTRIN should not be taken during pregnancy or by nursing mothers.

ADVERSE REACTIONS: The most frequent type of adverse reaction occurring with MOTRIN is gastrointestinal of which one or more occurred in 4% to 16% of the patients. Reported side effects were higher at 3200 than at 2400 mg/day or less.

Incidence Greater than 1% (but less than 3%)—Probable Causal Relationship

GASTROINTESTINAL: Nausea,* epigastric pain,* heartburn,* diarrhea, abdominal distress, nausea and vomiting, indigestion, constipation, abdominal cramps or pain, fullness of GI tract (bloating and flatulence); **CENTRAL NERVOUS SYSTEM:** Dizziness,* headache, nervousness; **DERMATOLOGIC:** Rash* (including maculopapular type), pruritus; **SPECIAL SENSES:** Tinnitus; **METABOLIC/ENDOCRINE:** Decreased appetite; **CARDIOVASCULAR:** Edema, fluid retention (generally responds promptly to drug discontinuation; see PRECAUTIONS).

Incidence less than 1% Probable Causal Relationship**

GASTROINTESTINAL: Gastric or duodenal ulcer with bleeding and/or perforation, gastrointestinal hemorrhage, melena, gastritis, hepatitis, jaundice, abnormal liver function tests; **CENTRAL NERVOUS SYSTEM:** Depression, insomnia, confusion, emotional lability, somnolence, aseptic meningitis with fever and coma; **DERMATOLOGIC:** Vesiculobullous eruptions, urticaria, erythema multiforme, Stevens-Johnson syndrome, alopecia; **SPECIAL SENSES:** Hearing loss, amblyopia (blurred and/or diminished vision, scotomata and/or changes in color vision) (see PRECAUTIONS); **HEMATOLOGIC:** Neutropenia, agranulocytosis, aplastic anemia, hemolytic anemia (sometimes Coombs positive), thrombocytopenia with or without purpura, eosinophilia, decreases in hemoglobin and hematocrit (see PRECAUTIONS); **CARDIOVASCULAR:** Congestive heart failure in patients with marginal cardiac function, elevated blood pressure, palpitations; **ALLERGIC:** Syndrome of abdominal pain, fever, chills, nausea and vomiting; anaphylaxis, bronchospasm (see CONTRAINDICATIONS); **RENAL:** Acute renal failure in patients with pre-existing significantly impaired renal function, decreased creatinine clearance, polyuria, azotemia, cystitis, hematuria; **MISCELLANEOUS:** Dry eyes and mouth, gingival ulcer, rhinitis.

Incidence less than 1%—Causal Relationship Unknown**

GASTROINTESTINAL: Pancreatitis; **CENTRAL NERVOUS SYSTEM:** Paresthesias, hallucinations, dream abnormalities, pseudotumor cerebri; **DERMATOLOGIC:** Toxic epidermal necrolysis, photoallergic skin reactions; **SPECIAL SENSES:** Conjunctivitis, diplopia, optic neuritis, cataracts; **HEMATOLOGIC:** Bleeding episodes (e.g. epistaxis, menorrhagia); **METABOLIC/ENDOCRINE:** Gynecomastia, hypoglycemic reaction, acidosis; **CARDIOVASCULAR:** Arrhythmias (sinus tachycardia, sinus bradycardia); **ALLERGIC:** Serum sickness, lupus erythematosus syndrome, Henoch-Schönlein vasculitis, angioedema; **RENAL:** Renal papillary necrosis.

*Reactions occurring in 3% to 9% of patients treated with MOTRIN. (Those reactions occurring in less than 3% of the patients are unmarked).

**Reactions are classified under "Probable Causal Relationship (PCR)" if there has been one positive challenge or if three or more cases occur which might be causally related. Reactions are classified under "Causal Relationship Unknown" if seven or more events have been reported but the criteria for PCR have not been met.

OVERDOSAGE: In cases of acute overdosage, the stomach should be emptied. The drug is acidic and excreted in the urine so alkaline diuresis may be beneficial.

DOSAGE AND ADMINISTRATION: Do not exceed 3200 mg/day.

Rheumatoid and osteoarthritis: Suggested dosage is 1200 to 3200 mg per day (400, 600 or 800 mg t.i.d. or q.i.d.). The smallest effective dosage should be used. Mild to moderate pain: 400 mg every 4 to 6 hours as necessary.

HOW SUPPLIED:

MOTRIN Tablets, 400 mg (orange)	MOTRIN Tablets, 600 mg (peach)	MOTRIN Tablets, 800 mg (apricot)
Bottles of 500	Bottles of 500	Bottles of 100
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Family Practice — no surgery	5,222
Family Practice — minor surgery or assisting at surgery	8,073
Family Practice — major surgery	17,905
General Surgery	17,905
Internal Medicine with invasive vascular procedures	10,924
Internal Medicine — no invasive vascular procedures	5,222
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Pediatrics — General, with invasive vascular procedures	10,924
Plastic Surgery, board certified	17,905
Psychiatry — no electro-convulsive therapy	2,371
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Radiology — including coronary angiography	10,924
Urology	13,775

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The following is a brief summary.

WARNING

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: Concomitant use with other potassium-sparing agents such as spironolactone or amiloride. Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K⁺ levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K⁺ intake. Associated widened QRS complex or arrhythmia requires prompt additional therapy. Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. Possible

exacerbation or activation of systemic lupus erythematosus has been reported with thiazide diuretics.

Precautions: The bioavailability of the hydrochlorothiazide component of 'Dyazide' is about 50% of the bioavailability of the single entity. Theoretically, a patient transferred from the single entities of triamterene and hydrochlorothiazide may show an increase in blood pressure or fluid retention. Similarly, it is also possible that the lesser hydrochlorothiazide bioavailability could lead to increased serum potassium levels. However, extensive clinical experience with 'Dyazide' suggests that these conditions have not been commonly observed in clinical practice. Angiotensin-converting enzyme (ACE) inhibitors can elevate serum potassium; use with caution with 'Dyazide'. Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids, and during concurrent use with amphotericin B or corticosteroids or corticotropin [ACTH]). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function. They can precipitate coma in patients with severe liver disease. Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic and hemolytic anemia have been reported with thiazides. Thiazides may cause manifestation of latent diabetes mellitus. The effects of oral anticoagulants may be decreased when used concurrently with hydrochlorothiazide; dosage adjustments may be necessary. Clinically insignificant reductions in arterial responsiveness to norepinephrine have been reported. Thiazides have also been shown to increase the paralyzing effect of nondepolarizing muscle relaxants such as tubocurarine. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. Triamterene has been found in renal stones in association with the other usual calculus components. Therefore, 'Dyazide' should be used with caution in patients with histories of stone formation. A few occurrences of acute renal failure have been reported in patients on 'Dyazide' when treated with indomethacin. Therefore, caution is advised in administering nonsteroidal anti-inflammatory agents with 'Dyazide'. The following

may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine. Hypokalemia is uncommon with 'Dyazide', but should it develop, corrective measures should be taken such as potassium supplementation or increased dietary intake of potassium-rich foods. Corrective measures should be instituted cautiously and serum potassium levels determined. Discontinue corrective measures and 'Dyazide' should laboratory values reveal elevated serum potassium. Chloride deficit may occur as well as dilutional hyponatremia. Concurrent use with chlorpropamide may increase the risk of severe hyponatremia. Serum PBI levels may decrease without signs of thyroid disturbance. Calcium excretion is decreased by thiazides. 'Dyazide' should be withdrawn before conducting tests for parathyroid function. Thiazides may add to or potentiate the action of other antihypertensive drugs. Diuretics reduce renal clearance of lithium and increase the risk of lithium toxicity.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances; postural hypotension (may be aggravated by alcohol, barbiturates, or narcotics); necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and respiratory distress including pneumonitis and pulmonary edema, transient blurred vision, sialadenitis, and vertigo have occurred with thiazides alone. Triamterene has been found in renal stones in association with other usual calculus components. Rare incidents of acute interstitial nephritis have been reported. Impotence has been reported in a few patients on 'Dyazide', although a causal relationship has not been established.

Supplied: 'Dyazide' is supplied as a red and white capsule, in bottles of 1000 capsules; Single Unit Packages (unit-dose) of 100 (intended for institutional use only); in Patient-Pak™ unit-of-use bottles of 100.

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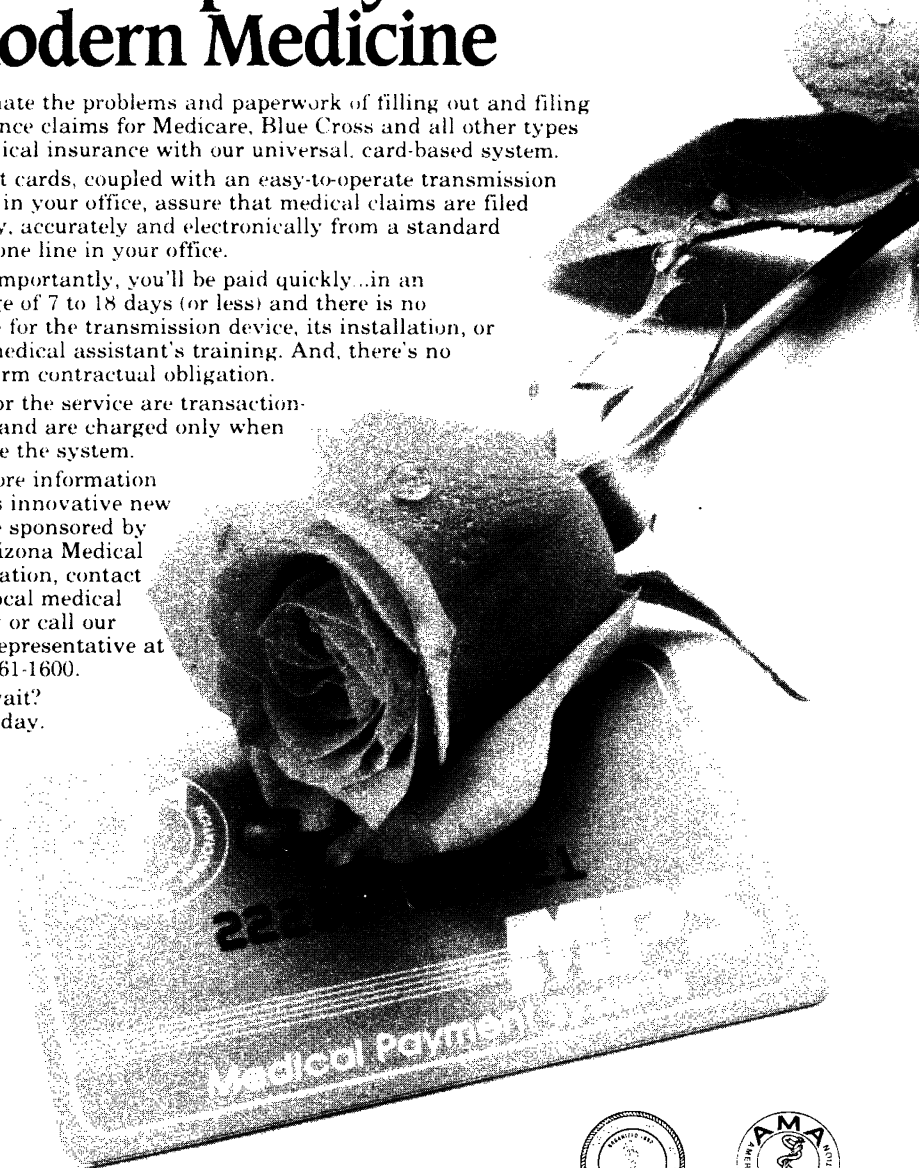
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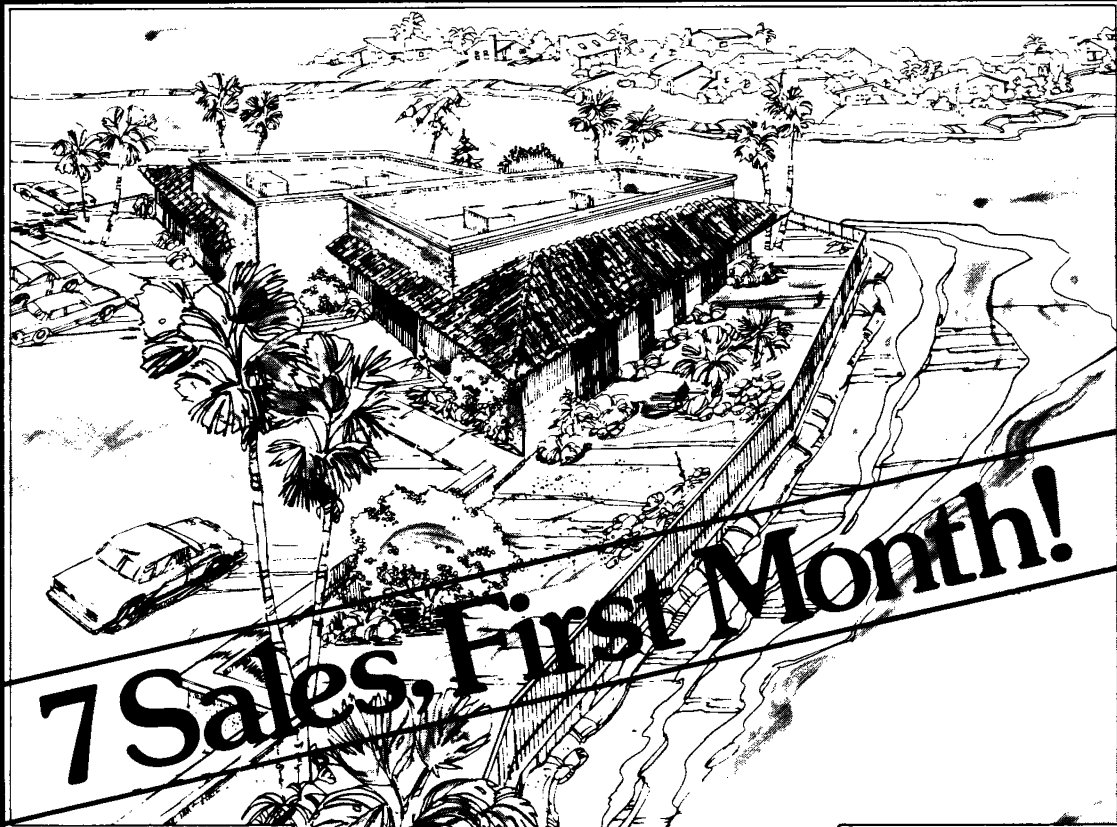


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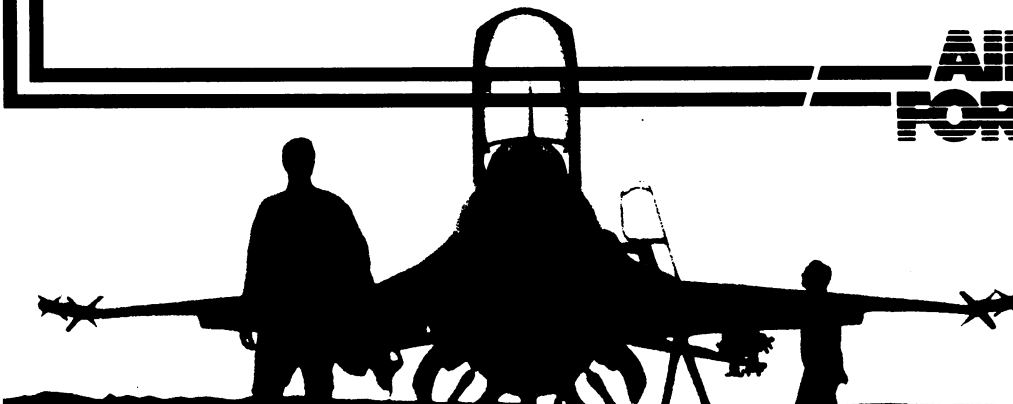
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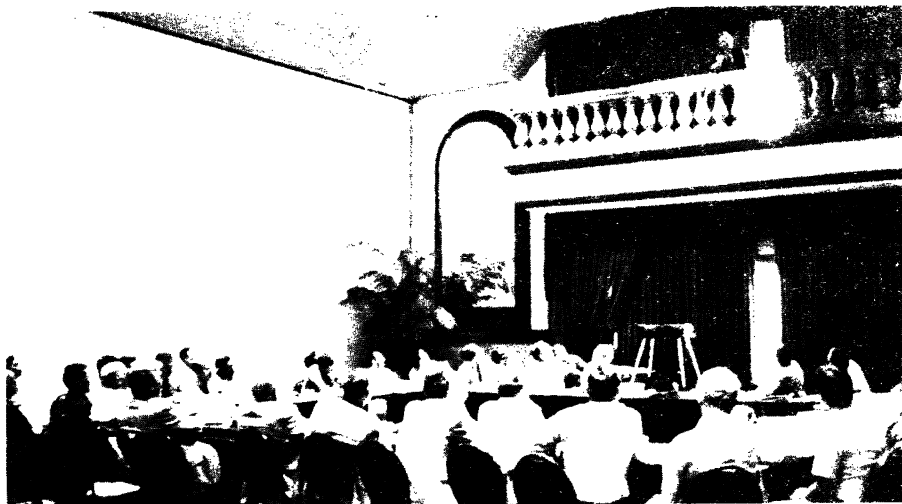
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Farewell

Outgoing ArMA President Neil O. Ward, M.D., of Phoenix responded to a "birthday request" from Board Attorney Edward Jacobson, Esq., and gave his farewell remarks from the balcony of the Board Meeting room.

ArMA's 96th Annual Meeting

The 96th Annual Meeting of The Arizona Medical Association's House of Delegates was held June 4, 5 and 6 at The Pointe at South Mountain, Phoenix. New officers and delegates to The American Medical Association were elected, as were alternate AMA delegates and members of the ArMA Board of Directors.



Auxiliary

The report on activities and accomplishments of the ArMA Auxiliary during the past year was given by Auxiliary President Jean Dew of Tucson.



Greetings

ArMA's new President, Robert S. Hirsch, M.D., of Tucson greeted members of the ArMA House of Delegates during their 1987 Annual Meeting. Seated are outgoing President Neil O. Ward, M.D., left, and Parliamentarian Charles Henderson, M.D., center.

Robert S. Hirsch, M.D., of Tucson was installed as ArMA's 1987-88 President; Richard L. Collins, M.D., of Scottsdale was elected President-Elect; Mark Ivey, Jr., M.D. of Payson was elected Vice President; Robert J. Brooks, M.D., of Tucson was elected Treasurer; and Richard O. Flynn, M.D., of Tempe was elected Vice-Speaker of the House.

AMA Delegates elected were Neopito L. Robles, M.D., of Tucson, Edward Sattenspiel, M.D., of Phoenix, and Richard D. Zonis, M.D., of Scottsdale. Alternate AMA Delegates elected were Paul T. Lenio, M.D., of Sierra Vista, Philip Levy, M.D., of Phoenix, and Walter K. Sosey, M.D., of Lake Havasu City.

Complete information about action taken by the Executive Committee, the Board of Directors and the House of Delegates on resolutions and Bylaw amendments is covered in a Medical Memo sent to all members of The Arizona Medical Association.



Legislature

Tort reform legislation approved, defeated and ready to return next year was reviewed by State Legislator Jim Meredith of Phoenix.

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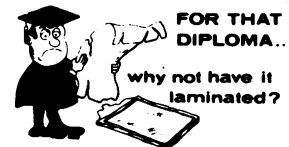
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Must see this exceptional 3-bedroom, 2½ bath, better-than-new custom home featuring two fireplaces, cathedral and vaulted ceilings, plant shelves and much more. Expansive master suite, split for privacy, custom designed security fenced pool. Cool neutral decor always immaculately maintained inside and out. Full tile roof and two-car garage. Offered at \$238,000. Call Linda O'Kelley at **John Hall & Associates**. (602) 948-0550.

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AZTEC CABINETS

Over ten years experience. Specializing in medical tenant improvements. Experienced in efficient office layout and design; top quality cabinets; scheduling and service are primary objectives; all styles of custom cabinets; new office furniture or will build to match existing; all types of wall paneling and mill work; also all types of residential work. References available upon request. (602) 968-0482.

FOR SALE

Well-maintained Del Mar Avionics Model 655 Holter Scanner and 3 Model 445 recorders as well as battery charger. \$60,000. Contact Mary Boehm (602) 848-5800

LARGE LOANS

Since 1966 specializing in large loans to physicians nationwide from \$15,000.00 to \$90,000.00. Long repayment terms at fixed interest rates. Commitments usually within 48 hours. Woodside Capital Corp., Woodside Capital Building, P.O. Box 368, Woodland Hills, CA 91365. For further information call (800) 423-5025.

PHYSICIANS SIGNATURE LOANS

Loans to \$50,000. Competitive fixed rates. No collateral. Up to seven years to repay with no pre-payment penalties. Prompt, courteous service. Physicians Service Association, Atlanta, Georgia (800) 241-6905. Serving MDs for over ten years.

Classified ad rates are \$20 for the first 50 words or less and 20 cents for each additional word. Send to: ArMA, 810 West Bethany Home Road, Phoenix, Arizona 85013.

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The rate for each insertion is **\$6 per line** (average six words per line) with **five line (\$30) minimum**. Box number charge: \$5 each month.

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CLASSIFIED ADVERTISEMENTS
THE WESTERN JOURNAL OF MEDICINE
P.O. BOX 7602, SAN FRANCISCO, CA 94120-7602

PHYSICIANS WANTED

ADDITIONAL INTERNIST NEEDED for busy 5-physician multispecialty group. Beautiful, well-equipped six-year-old office just 75 feet from 34-bed hospital with ICU/CCU unit. This all Board certified group houses three Family Practitioners, two General Surgeons, and one Internist. Coastal retirement town offers top-notch school system and excellent array of activities. Located just 75 easy miles from Portland adds even more cultural and shopping opportunities. For further information contact Rick Bigger days at North Coast Medical Center, PC, Seaside, Oregon; (503) 738-9551.

NORTHERN CALIFORNIA. FP/IM physicians needed to staff ambulatory care clinics in the Central Valley region of California. Paid malpractice and excellent benefit package. Incentive plus guarantee. If interested, please contact SEMG, PO Box 214584, Sacramento, CA 95821.

PRACTICE FAMILY MEDICINE with the people in rural Iowa communities where the quality of life is superb. Solo and group practice opportunities available including guaranteed salaries and full benefit packages. For an immediate response please call 1 (800) 247-3121, ext 8204 (USA).

NEW MEXICO—TAOS AND LAS VEGAS. Excellent full-time hospital emergency department positions are currently available with Spectrum in Taos and Las Vegas. Moderate to low volume emergency departments. Excellent medical and nursing support. Guaranteed rate of reimbursement, occurrence malpractice insurance coverage, CME allowance, reimbursement of professional dues. For additional information on these opportunities, contact Beth Sheldahl, Spectrum Emergency Care, 6275 Lehman Dr, Ste C202, Colorado Springs, CO 80918; 1 (800) 525-3681; (303) 590-1755.

CALIFORNIA, SAN FRANCISCO BAY AREA. A leading HMO near San Francisco, California is seeking Board prepared/certified physicians to staff a busy, urban, full-service Emergency Department. Kaiser Permanente is a large, pre-paid Health Maintenance Organization offering a competitive salary, job security, shareholder status, and generous benefits including health care, life insurance, disability insurance, sick leave, and educational leave. Please address all inquiries to Hans P. Odsen, MD, Chief, Emergency Department, Kaiser Permanente Medical Center, 1200 El Camino Real, South San Francisco, CA 94080; (415) 742-2513 or 2514.

PHYSICIANS WANTED

OREGON. General Internist sought for busy practice. Multispecialty group of 10 physicians, 38 miles from Portland. CV to Administrator, Physicians' Medical Center, PC, 420 E. Fifth St, McMinnville, OR 97128; (503) 472-6161.

PHYSIATRIST—BC/BE for northern California practice oriented towards clinical, occupational and evaluative medicine; qualified applicants will have EMG/NCS, EEG experience, be familiar with med-legal environment and seek a growth oriented opportunity; send current CV, letter of interest and compensation requirements to Box 164, 1550 California St, Ste 6, San Francisco, CA 94109.

CHIEF OF PEDIATRICS. Natividad Medical Center, a University of California, San Francisco affiliated hospital, located in beautiful Monterey County, is seeking a BC/BE Pediatrician. Preference given to physician with Chief Residency or subspecialty experience. Natividad sponsors a family practice residency program with 18 residents. Salary range from \$73,000 to \$78,000 depending upon qualifications with excellent benefit package. Natividad Medical Center is an Affirmative Action Equal Opportunity Employer. For further information, please mail CV or contact Richard McClurkin, Personnel Officer/Search Board Leader, PO Box 8-1611, Salinas, CA 93912-1611; (408) 757-0581.

FAMILY PRACTITIONER. Full-time BE/BC FP for growing multispecialty group in sunny California. Some Spanish helpful. First year compensation, benefits, and malpractice. Partnership potential second year. Send CV to Number 29, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

ORTHOPEDIC SURGEON. Natividad Medical Center, a University of California, San Francisco affiliated hospital, located in beautiful Monterey County, is recruiting an Orthopedic Surgeon. This position combines teaching and practice. The hospital sponsors a family practice residency program with 18 residents and has a very active trauma service with a regional paramedic base station. An attractive base salary with fee-for-service incentive option is negotiable. Natividad Medical Center is an Affirmative Action Equal Opportunity Employer. For further information, please mail CV or contact: Richard McClurkin, Personnel Officer/Search Board Leader, PO Box 8-1611, Salinas, CA 93912-1611; (408) 757-0581.

PHYSICIANS WANTED

SOUTHERN CALIFORNIA

Enjoy professional challenge and growth with a successful and expanding HMO in Southern California. CIGNA Healthplans of California is seeking Specialists and Primary Care physicians committed to concepts of prevention and health maintenance to join our facilities in Los Angeles and Orange Counties. We offer an excellent compensation and benefits package including profit sharing. For consideration, please forward CV to:

Director/Physician Recruitment
CIGNA Healthplans of California
505 N. Brand Blvd, Suite 400-49
Glendale, CA 91203

NEAR STANFORD. Six Internists, all sub-specialty trained and members of clinical faculty at Stanford, interested in an Associate with subspecialty interest and training. Should be well grounded in Internal Medicine. Send CV to Dr Bigler, El Camino Internal Medical Group, 125 South Dr, Mountain View, CA 94040.

OREGON. Emergency department Medical Director and full-time Staff Physician are needed at client hospital located in community on the Columbia River in north central Oregon. Full service community hospital with moderate volume emergency department. Guaranteed rate of reimbursement, occurrence malpractice insurance coverage, CME allowance, reimbursement of professional dues, plus directors receive paid health benefits which include dependents. For additional information on this opportunity, contact Bill Salmo, Spectrum Emergency Care, 6275 Lehman Dr, Ste C202, Colorado Springs, CO 80918; 1 (800) 525-3681; (303) 590-1755.

MD NEEDS—OB/GYN and IM or IM/Oncologist needed for a multispecialty group practice in Helena, Montana. Capital of state, population 30,000-35,000, small private college, close to Rocky Mountains with fishing, hunting and outdoor sports. Midway between Glacier and Yellowstone Parks. Reply to Dan B. Smelko, Helena Medical Clinic, PC, 1930 9th Ave, Helena, MT 59601.

FAMILY PRACTICE. Excellent professional opportunity in beautiful north Idaho. Nominal lease at hospital owned clinic includes fully-equipped office, treatment suites and general receptionist. X-ray, lab and pharmacy on site. Located in 4-season playground rich with recreational opportunities. For information call Nancy at (208) 784-1221, ext 304, or send resumé to Shoshone Medical Center, Jacobs Gulch, Kellogg, ID 83837.

ORTHOPEDIC SURGEON. Full-time Orthopedic Surgeon to join growing multispecialty group in sunny California. Salary, incentive, malpractice and benefits. Great potential for right physician. Individual ownership. Send CV to Number 30, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

INTERNAL MEDICINE. Full-time BE/BC active Internist for multispecialty group in sunny California. Office/hospital and consult practice. Spanish a plus. Salary, benefits, and malpractice. Potential for partnership second year. Send CV to Number 31, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

CALIFORNIA FORENSIC MEDICAL GROUP, INC. a corporation providing medical services in California county jails, has opportunities for physicians with a specialty in either Family Practice, General Practice or Internal Medicine. Send resumé to CFMG, Inc, PO Box 1831, Salinas, CA 93902; or contact Elaine Hustedt (408) 422-0214.

WE HAVE FULL- AND PART-TIME LOCUM TENENS opportunities available with guaranteed incomes and paid malpractice. For more information, contact John Smith, Locum Tenens, Inc (A Division of Jackson and Coker), 400 Perimeter Center Terrace, Ste 760 WJM, Atlanta, GA 30346; Tel. 1 (800) 544-1987.

(Continued on Page 114)



CNA has a longstanding commitment to medical malpractice protection.

The CNA Insurance Companies have been committed to providing quality malpractice insurance for over 15 years. And we've kept this commitment even through the years of malpractice crises.

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211 Sixth Avenue, North
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(Continued from Page 112)

PHYSICIANS WANTED

NORTHERN CALIFORNIA, EMERGENCY MEDICINE. Full-time positions available in the Emergency Department at the University of California, Davis, Medical Center. The University serves a large region of northern California and is a major trauma center. Emergency physicians teach and supervise medical students and housestaff (240 per year) in addition to treating patients. Emergency Department physicians also provide medical control for UCDCMC Life Flight, director of base station activities, and are actively involved in trauma care. Opportunities exist for involvement in other UCD School of Medicine teaching activities. Applicants should send CV to Robert W. Derlet, MD, Chief, Division of Emergency Medicine, University of California, Davis, Medical Center, 2315 Stockton Blvd, Sacramento, CA 95817.

MINNEAPOLIS. Seeks BC/BE associates in Adult Psychiatry, Cardiology, Family Practice, Internal Medicine, Obstetrics and Gynecology and Urology. Practice quality medicine in a prepaid multispecialty setting located in one of America's leading metropolitan areas. Comprehensive benefits, excellent facilities, flexible compensation programs. For further information about joining the Group Health medical staff, call Jerry Hess at (612) 623-8444 or write to Group Health, Inc, Attn: Jerry Hess, 2829 University Ave, SE, Minneapolis, MN 55414.

SALT LAKE AREA. General Practitioner needed for new, fully-equipped facility. Excellent salary—benefit package, plus percentage. Enjoy outdoor recreation, skiing, hunting, fishing, as well as cosmopolitan living. Reply to Number 34, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

GENERAL SURGEON. Excellent opportunity for BC/BE in General Surgery. Close to San Francisco in beautiful wine country. Reply to Number 38, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

MULTISPECIALTY GROUP in San Francisco bay area looking for Board certified Family Practitioner for beautiful satellite office. Competitive salary and later incentive program. Contact David Louis, MD, 3100 Telegraph Ave, Oakland, CA 94609; (415) 273-8150.

CALIFORNIA, SAN FRANCISCO BAY AREA. Full-time career Emergency Physician wanted for high-volume Emergency Department. Emergency Medicine Board certified or Board-ready mandatory to participate in a group of 20 full-time staff physicians seeing over 300 patients per day. Salaried position, excellent benefits include three weeks paid vacation; one week CME; paid malpractice, health and life insurance; corporate shareholdership in three years. Send CV or contact David Gallagher, MD, 27400 Hesperian Blvd, Hayward, CA 94545.

ARIZONA-BASED PHYSICIAN recruiting firm has opportunities coast-to-coast. "Quality Physicians for Quality Clients since 1972." Call (602) 990-8080; or send CV to Mitchell & Associates, Inc, PO Box 1804, Scottsdale, AZ 85252.

NEONATOLOGIST. Member of 28-physician, multispecialty group in North Dakota. 250-bed hospital with fully-equipped Level III unit. Excellent salary plus bonus. Contact Jean Malkasian, 250 Regency Ct, Waukesha, WI 53186, or (414) 785-6500, collect.

CORPORATE MEDICINE FOUR OPENINGS

Major southern California company needs two Associate Medical Directors (Gerontology Director and Cardiac Risk Manager), Internist, and Industrial. Salary \$75K to \$130K plus lucrative benefits. WSPS, 407 S. Clovis Ave, Ste 108, Fresno, CA 93727; (209) 252-3000.

PHYSICIANS WANTED

WASHINGTON STATE

The Wenatchee Valley Clinic, a multispecialty group of 105 physicians, has several practice opportunities throughout its seven practice locations. Currently we are seeking:

MAIN FACILITY—WENATCHEE

- Pediatrics
- Allergy
- Nephrology
- Psychiatry
- General Internal Medicine

SATELLITE FACILITIES—OMAK/MOSES LAKE

- Orthopedics
- General Surgery
- General Internal Medicine
- OB/GYN
- Radiology

All positions offer an excellent compensation and benefit package. North central Washington provides a high quality of life for those interested in an abundance of recreational opportunities in a family-oriented rural setting. If interested, send your CV to Dr Gerald Gibbons, Medical Director, Wenatchee Valley Clinic, 820 N. Chelan Ave, Wenatchee, WA 98801, or call (509) 663-8711, ext 205.

WYOMING—EMERGENCY MEDICINE. Immediate opening. Full-time ER Physician. Pleasant working conditions. New hospital. Competitive compensation. Flexible scheduling. Paid malpractice. Small community life-style. Excellent outdoor recreation: camping, hunting, fishing, skiing and more. 72 miles to Salt Lake City. Send CV to Steven P. French, MD, Director, Emergency Department, 190 Arrowhead Dr, Evanston, WY 82930; (307) 789-3636.

WORK PART-TIME. Position available for Internist or GP/FP with Internal Medicine experience in Primary Care Practice, northern California Sierra foothills community of 25,000. Share rotating practice with two other MDs; you work one week in three. Outpatient and inpatient responsibilities (no OB, no ICU) in modern, fully-equipped 100-bed hospital. Minimum salary of \$1,800/week (with incentives, actual will be around \$2,200/week). Insurance, housing, and meals provided N/C. Send CV to David Lomba, 133 'B' Ascot Ct, Moraga, CA 94556.

PHYSICIAN OPENING. Ambulatory care/minor emergency center. Full- or part-time for FP/IM/EM trained/experienced physician. Located in Tacoma area. Flexible scheduling, pleasant setting, quality medicine. Contact David R. Kennel, MD, 5900-100th St SW, Ste 31, Tacoma, WA 98499; (206) 584-3023 or (206) 582-2542.

THE IRVINE MEDICAL CENTER and the University of California, Irvine, Department of Radiological Sciences are seeking a full-time faculty member for the Department of Radiological Sciences at the Clinical Assistant or Associate Professor level who would be assigned as Director of the Department of Radiology at Irvine Medical Center. The Irvine Medical Center is a new 177-bed hospital currently under construction in Irvine, California. Hospital opening is scheduled for fall of 1988. Administrative experience and academic background, including teaching and/or research, are required. Please send CV and the names of five references to Richard M. Friedenberg, MD, Professor and Chairman, Department of Radiological Sciences, University of California, Irvine, 101 City Dr South, Orange, CA 92668. The University of California is an affirmative action and an equal opportunity employer.

CALIFORNIA, MERCED. Emergency Department medical directorship and full-time staff opportunities are available at our client hospital in Merced. Full-service community hospital with moderate volume ED. Guaranteed rate of compensation, occurrence malpractice insurance coverage, CME allowance, reimbursement of professional dues, relocation allowance. Must be willing to live in community. For additional details contact Bill Salmo, Spectrum Emergency Care, 6275 Lehman Dr, Ste C-202, Colorado Springs, CO 80918; (800) 525-3681; (303) 590-1755.

PHYSICIANS WANTED

ORTHOPEDIC SURGEON. Opportunities throughout the midwest and Colorado. These positions offer both general orthopedic practices, along with subspecialized training. Partnership and group settings. Contact Jean Malkasian, 250 Regency Ct, Waukesha, WI 53186; (414) 785-6600, collect.

ANESTHESIOLOGIST sought for the Española Hospital in Española, New Mexico. Financial assistance with income guarantee. For further information, please submit CV to Bill Norris, Southwest Community Health Services, PO Box 26666, Albuquerque, NM 87125-6666; or call 1 (800) 545-4030, ext 8300.

MEDICAL OFFICER (OCCUPATIONAL MEDICINE). GM-602-13, salary range \$45,117 to \$56,394; Naval Medical Clinic, Occupational Medical Branch, Port Hueneme, California; send résumés to NCBC, Code 231 (M. Presley), Bldg 14, Rm 157, Port Hueneme, CA 93043-5000; or call (805) 982-4473.

INTERNAL MEDICINE. San Francisco suburb. BC/BE associate needed for busy solo practice adjacent to Mount Diablo Hospital. Send CV to Number 41, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

INTERNIST position available with 35 member multispecialty group; BC/BE; immediate opening; full range of benefits plus immediate shareholder status; excellent opportunity; central coast of California. Respond with CV to Colin J. Wells, MD, San Luis Medical Clinic, Ltd, 1235 Osos St, San Luis Obispo, CA 93401-3619. NO PHONE CALLS PLEASE.

FAMILY PHYSICIAN. BC/BE, residency-trained, to join group in Santa Fe, New Mexico. Practice includes obstetrics and after-hours care. \$40,000, incentive. Reply to Number 46, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

PEDIATRICIANS/UTAH and COLORADO. Join two Pediatricians in Layton, Utah, 20 miles north of Salt Lake City. There is also a solo opportunity in Thornton, Colorado, a northern suburb of Denver. For further information, call or send your CV to Gordon Crawford, Humana Inc, Dept. G-7, 500 West Main St, Louisville, KY 40201-1438. Toll-free: (800) 626-1590.

MEDICAL DIRECTOR. Progressive, growth oriented, multispecialty, nonprofit corporation is seeking a full-time Medical Director. The Director will be responsible for the supervision of a comprehensive medical program that includes x-ray, laboratory, pharmacy. Candidates for the position must have graduated from an accredited medical school and have strong clinical as well as administrative skills. Family Practice specialty with Board certification is preferred. Excellent salary and benefit package available. For more information send CV to Jack Hicks, Assistant Director, Operations/Personnel, Clinica Sierra Vista, PO Box 457, Lamont, CA 93241; (805) 845-3731.

FAMILY PRACTICE. Associate sought for growing, solo, woman-owned southern California family practice in Orange County, near beach. Warm office. Hard work. No OB. Early partnership. Spanish helpful. Leave message, (714) 497-4276.

WESTERN STATES OPENINGS

Many multispecialty groups and hospitals have asked us to recruit for over 300 positions of various specialties.

Western States Physician Services
407 S. Clovis Ave, Ste 108
Fresno, CA 93727; (209) 252-3000

(Continued on Page 116)

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PHYSICIANS WANTED**HOUSE PHYSICIANS**

These day and evening openings allow you to practice in our comfortably-sized, 200-bed acute care hospital in a beautiful San Francisco neighborhood. Positions start July 1 and cover ICU patients. Direct inquiries to Dr Rosenstein, (415) 386-7000.

**MARSHAL HALE
MEMORIAL HOSPITAL**

FAMILY PRACTICE IN IDAHO? Join four physicians and nine nurse practitioners in an exciting clinic system. One position available in September 1987. Attractive salary and benefit package. Contact Erwin B. Teuber, PhD, Administrator, or Robert LeBow, MD, Medical Director, Terry Reilly Health Services, 211 16th Ave North, Nampa, ID 83651; (208) 467-4431.

IDAHO NEEDS FULL-TIME EMERGENCY PHYSICIAN. 20 miles from Boise, near mountains and unlimited recreation. Excellent opportunity to affiliate with 162-bed hospital. ACLS-yes. Contact M. Kutsurelis, Vice President Administrative Services, Mercy Medical Center, 1512 12th Ave Road, Nampa, ID 83651; (208) 467-1171.

FEMALE FAMILY PRACTITIONER wants help caring for young, healthy families. Some obstetrics, flexible schedule; possible temporary or permanent partnership. PO Box 819, Mendocino, CA 95460; (707) 937-4272.

LAKEWOOD HOSPITAL, SOUTH PUGET SOUND, recruiting for associates in: Family Practice and Internal Medicine; is a 95-bed acute care surgical, medical, and obstetrical hospital which has a new facility due for early 1988 completion. In addition, a very busy associate physician wishes to retire from his solo practice in Internal Medicine. This practice, which was established and has run consistently since 1966, is for sale. Lakewood is the "Lake District" of south Puget Sound surrounded by the Olympic Mountains, the Cascades and Mt. Rainier which provide outstanding water and mountain recreational activities. BC/BE respond to Genie Latta, Physician Recruitment, Lakewood Hospital, 5702 100th St S.W., Tacoma, WA 98499-0998; (206) 588-1711.

THE COMMUNITY OF ARTESIA, NEW MEXICO is seeking a Board certified or eligible General Surgeon to establish a private practice. Fully-equipped office with established referral patterns available for purchase. Community-based financial assistance may be available to the right individual. Artesia is a community of 14,000 located in southeast New Mexico. A great place to raise a family—peaceful community with year 'round recreation and excellent weather. Fully-equipped, 38-bed new hospital. Please submit CV to Bill Norris, Southwest Community Health Services, PO Box 26666, Albuquerque, NM 87125-6666; or call 1 (800) 545-4030, ext 8300.

GENERAL SURGEON BC/BE. Excellent opportunity to associate in a busy surgical practice in Sonoma, California, one hour drive north of San Francisco. Contact J. Basil Haddad, MD, 181 Andrieux St, Sonoma, CA 95476; (707) 996-6119.

EXCELLENT TEXAS OPPORTUNITIES. ENT, Family Practitioner, General Practitioner, General Surgeon, Internal Medicine, OB/GYN person, Ophthalmologist, Oncologist, Pediatrician, Radiation Oncologist to practice in one of several lake area communities, in the beautiful Piney Woods area of east Texas. Enjoy boating, fishing, hunting year 'round. Excellent quality of life, first year guarantee, etc. Other Texas opportunities available also. Reply with CV to Medical Support Services, Armando L. Frezza, 11509 Quarter Horse Trail, Austin, TX 78750; (512) 331-4164.

(Continued on Page 120)

THE ARMY NEEDS PHYSICIANS PART-TIME.



If you are a practicing physician who wants a break from your daily practice . . . while still practicing high-quality medicine and serving your country . . . consider an officer commission in the ARMY RESERVE MEDICAL CORPS.

AMONG THE BENEFITS:

- Subsidized professional development which could include two conferences/short courses of your choice.
- Up to \$50,000 Group Life Insurance package, nominally priced for qualifying MD's, generous retirement annuity to qualifying physicians at age 60.
- Monthly stipend for local professional services.
- Post Exchange, Commissary (during Annual Training) and space-available travel on military aircraft.
- Flexible training programs that won't interfere with your practice.

To see if you qualify contact:

Major Patricia S. Schackleton, MSC 415-751-1616

Major Michael F. Lyons, MSC 213-474-0138

Captain Gregory F. Linden, MSC 619-453-9937

News from  about a new dosage form of cephalixin

ANNOUNCING NEW

KefletTM TABLETS cephalexin

All the advantages of cephalixin in a convenient tablet form

- Backed by over 15 years of clinical experience
- Smaller tablet is specially shaped and coated for easier swallowing
- May enhance patient compliance, particularly among the elderly
- Tablet dosage form may be appreciated by patients of all ages

NEW Keflet Tablets are available as:

250-mg
Tablets

KEFLET
250



500-mg
Tablets

Keflet is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-sensitive patients.

Brief Summary. Consult the package literature for prescribing information.

Indications and Usage: KefletTM Tablets (cephalexin, Dista) are indicated for the treatment of the following infections when caused by susceptible strains of the designated microorganisms:

Respiratory tract infections caused by *Streptococcus pneumoniae* and group A β -hemolytic streptococci (Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. Keflet is generally effective in the eradication of streptococci from the nasopharynx; however, substantial data establishing the efficacy of Keflet in the subsequent prevention of rheumatic fever are not available at present.)

Otitis media due to *S. pneumoniae*, *Haemophilus influenzae*, staphylococci, streptococci, and *Neisseria catarrhalis*

Skin and skin structure infections caused by staphylococci and/or streptococci

Bone infections caused by staphylococci and/or *Proteus mirabilis*

Genitourinary tract infections, including acute prostatitis, caused by *Escherichia coli*, *P. mirabilis*, and *Klebsiella* sp.

Note:—Culture and susceptibility tests should be initiated prior to and during therapy. Renal function studies should be performed when indicated.

Contraindication: Keflet is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

Warnings: BEFORE CEPHALEXIN THERAPY IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE CONCERNING PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS AND PENICILLIN. CEPHALOSPORIN C DERIVATIVES SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS.

SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE EPINEPHRINE AND OTHER EMERGENCY MEASURES.

There is some clinical and laboratory evidence of partial cross-allergenicity of the penicillins and the cephalosporins. Patients have been reported to have had severe reactions (including anaphylaxis) to both drugs.

Any patient who has demonstrated some form of allergy, particularly to drugs, should receive antibiotics cautiously. No exception should be made with regard to Keflet.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics (including macrolides, semisynthetic penicillins, and cephalosporins); therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with the use of antibiotics. Such colitis may range in severity from mild to life-threatening.

Treatment with broad-spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis.

Mild cases of pseudomembranous colitis usually respond to drug discontinuance alone. In moderate to severe cases, management should include sigmoidoscopy, appropriate bacteriologic studies, and fluid, electrolyte, and protein supplementation. When the colitis does not improve after the drug has been discontinued, or when it is severe, oral vancomycin is the drug of choice for antibiotic-associated pseudomembranous colitis produced by *C. difficile*. Other causes of colitis should be ruled out.

Usage in Pregnancy:—Safety of this product for use during pregnancy has not been established.

Precautions: **General:**—Patients should be followed carefully so that any side effects or unusual manifestations of drug idiosyncrasy may be detected. If an allergic reaction to Keflet occurs, the drug should be discontinued and the patient treated with the usual agents (e.g., epinephrine or other pressor amines, antihistamines, or corticosteroids).

Prolonged use of Keflet may result in the overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs' testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognized that a positive Coombs' test may be due to the drug.

Keflet should be administered with caution in the presence of markedly impaired renal function. Under such conditions, careful clinical observation and laboratory studies should be made because safe dosage may be lower than that usually recommended.

Indicated surgical procedures should be performed in conjunction with antibiotic therapy.

As a result of administration of Keflet, a false-positive reaction for glucose in the urine may occur. This has been observed with Benedict's and Fehling's solutions and also with Clinistix[®] tablets but not with Tes-Tape[®] (Glucose Enzymatic Test Strip, USP, Lilly).

Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Usage in Pregnancy—Pregnancy Category B:—The daily oral administration of cephalixin to rats in doses of 250 or 500 mg/kg prior to and during pregnancy, or to rats and mice during the period of organogenesis only, had no adverse effect on fertility, fetal viability, fetal weight, or litter size. Note that the safety of cephalixin during pregnancy in humans has not been established.

Cephalexin showed no enhanced toxicity in weanling and newborn rats as compared with adult animals. Nevertheless, because the studies in humans cannot rule out the possibility of harm, Keflet should be used during pregnancy only if clearly needed.

Nursing Mothers:—The excretion of cephalixin in the milk increased up to 4 hours after a 500-mg dose; the drug reached a maximum level of 4 µg/mL, then decreased gradually, and had disappeared 8 hours after administration. Caution should be exercised when Keflet is administered to a nursing woman.

Adverse Reactions: **Gastrointestinal:**—Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment. Nausea and vomiting have been reported rarely. The most frequent side effect has been diarrhea. It was very rarely severe enough to warrant cessation of therapy. Dyspepsia and abdominal pain have also occurred. As with some penicillins and some other cephalosporins, transient hepatitis and cholestatic jaundice have been reported rarely.

Hypersensitivity:—Allergic reactions in the form of rash, urticaria, angioedema, and, rarely, erythema multiforme, Stevens Johnson Syndrome, or toxic epidermal necrolysis have been observed. These reactions usually subsided upon discontinuation of the drug. Anaphylaxis has also been reported.

Other reactions have included genital and anal pruritus, genital moniliasis, vaginitis and vaginal discharge, dizziness, fatigue, and headache. Eosinophilia, neutropenia, thrombocytopenia, and slight elevations in SGOT and SGPT have been reported.

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Additional information available to the profession on request from



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(Continued from Page 117)

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INTERNIST, ENDOCRINOLOGIST, BE, trained at UCSF, outpatient clinical experience, desires position consisting of General Internal Medicine and specialty. Reply to Number 47, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

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(Continued on Page 122)

(Continued from Page 120)

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Rocephin® IV·IM

ceftriaxone sodium/Roche

Before prescribing, please consult complete product information, a summary of which follows:

MICROBIOLOGY: The bactericidal activity of ceftriaxone results from inhibition of cell wall synthesis. Ceftriaxone has a high degree of stability in the presence of beta-lactamases, both penicillinases and cephalosporinases, of gram-negative and gram-positive bacteria. Ceftriaxone is usually active against the following microorganisms *in vitro* and in clinical infections (see Indications and Usage).

GRAM-NEGATIVE AEROBES: *Enterobacter aerogenes*, *Enterobacter cloacae*, *Escherichia coli*, *Haemophilus influenzae* (including ampicillin-resistant strains), *H. parainfluenzae*, *Klebsiella* species (including *K. pneumoniae*), *Neisseria gonorrhoeae* (including penicillinase and nonpenicillinase producing strains), *Neisseria meningitidis*, *Proteus mirabilis*, *Proteus vulgaris*, *Morganella morganii* and *Serratia marcescens*.

Note: Many strains of the above organisms that are multiply resistant to other antibiotics, e.g., penicillins, cephalosporins and aminoglycosides, are susceptible to ceftriaxone sodium.

Ceftriaxone is also active against many strains of *Pseudomonas aeruginosa*.

GRAM-POSITIVE AEROBES: *Staphylococcus aureus* (including penicillinase producing strains) and *Staphylococcus epidermidis* (Note: methicillin-resistant staphylococci are resistant to cephalosporins, including ceftriaxone). *Streptococcus pyogenes* (Group A beta-hemolytic streptococci), *Streptococcus agalactiae* (Group B streptococci) and *Streptococcus pneumoniae*. (Note: Most strains of enterococci, *Streptococcus faecalis* and Group D streptococci are resistant.)

Ceftriaxone also demonstrates *in vitro* activity against the following microorganisms, although the clinical significance is unknown.

GRAM-NEGATIVE AEROBES: *Citrobacter freundii*, *Citrobacter diversus*, *Providencia* species (including *Providencia rettgeri*), *Salmonella* species (including *S. typhi*), *Shigella* species and *Acinetobacter calcoaceticus*.

ANAEROBES: *Bacteroides* species, *Clostridium* species (Note: most strains of *C. difficile* are resistant).

SUSCEPTIBILITY TESTING: Standard susceptibility disk method. Quantitative methods that require measurement of zone diameters give the most precise estimate of antibiotic susceptibility. One such procedure (Bauer AW, Kirby WMM, Sherris JC, Turck M: Antibiotic Susceptibility Testing by a Standardized Single Disk Method, *Am J Clin Pathol* 45:493-496, 1966; Standardized Disk Susceptibility Test, *Federal Register* 39:19182-19184, 1974; National Committee for Clinical Laboratory Standards, Approved Standard, ASM 2: Performance Standards for Antimicrobial Disk Susceptibility Tests, July 1975) has been recommended for use with disks to test susceptibility to ceftriaxone.

Laboratory results of the standardized single-disk susceptibility test using a 30 mcg ceftriaxone disk should be interpreted according to the following three criteria:

1. Susceptible organisms produce zones of 18 mm or greater, indicating that the tested organism is likely to respond to therapy.
2. Organisms that produce zones of 14 to 17 mm are expected to be susceptible if a high dosage (not to exceed 4 gm per day) is used or if the infection is confined to tissues and fluids (e.g., urine), in which high antibiotic levels are attained.
3. Resistant organisms produce zones of 13 mm or less, indicating that other therapy should be selected.

Organisms should be tested with the ceftriaxone disk, since ceftriaxone has been shown by *in vitro* tests to be active against certain strains found resistant to cephalosporin class disks.

Organisms having zones of less than 18 mm around the cephalothin disk are not necessarily of intermediate susceptibility or resistant to ceftriaxone.

Standardized procedures require use of control organisms. The 30-mcg ceftriaxone disk should give zone diameters between 29 and 35 mm, 22 and 28 mm and 17 and 23 mm for the reference strains *E. coli* ATCC 25922, *S. aureus* ATCC 25923 and *P. aeruginosa* ATCC 27853, respectively.

DILUTION TECHNIQUES: Based on the pharmacokinetic profile of ceftriaxone, a bacterial isolate may be considered susceptible if the MIC value for ceftriaxone is not more than 16 mcg/ml. Organisms are considered resistant to ceftriaxone if the MIC is equal to or greater than 64 mcg/ml. Organisms having an MIC value of less than 64 mcg/ml, but greater than 16 mcg/ml, are expected to be susceptible if a high dosage (not to exceed 4 gm per day) is used or if the infection is confined to tissues and fluids (e.g., urine), in which high antibiotic levels are attained.

E. coli ATCC 25922, *S. aureus* ATCC 25923 and *P. aeruginosa* ATCC 27853 are also the recommended reference strains for controlling ceftriaxone dilution tests. Greater than 95% of MICs for the *E. coli* strain should fall within the range of 0.016 to 0.5 mcg/ml. The range for the *S. aureus* strain should be 1 to 2 mcg/ml, while for the *P. aeruginosa* strain the range should be 8 to 64 mcg/ml.

INDICATIONS AND USAGE: Rocephin is indicated for the treatment of the following infections when caused by susceptible organisms.

LOWER RESPIRATORY TRACT INFECTIONS caused by *Strep. pneumoniae*, *Streptococcus* species (excluding enterococci), *Staph. aureus*, *H. influenzae*, *H. parainfluenzae*, *Klebsiella* species (including *K. pneumoniae*), *E. coli*, *E. aerogenes*, *Proteus mirabilis* and *Serratia marcescens*.

SKIN AND SKIN STRUCTURE INFECTIONS caused by *Staph. aureus*, *Staph. epidermidis*, *Streptococcus* species (excluding enterococci), *E. cloacae*, *Klebsiella* species (including *K. pneumoniae*), *Proteus mirabilis* and *Pseudomonas aeruginosa*.

URINARY TRACT INFECTIONS (complicated and uncomplicated) caused by *E. coli*, *Proteus mirabilis*, *Proteus vulgaris*, *M. morganii* and *Klebsiella* species (including *K. pneumoniae*).

UNCOMPLICATED GONORRHEA (cervical, urethral and rectal) caused by *Neisseria gonorrhoeae*, including both penicillinase and nonpenicillinase producing strains.

PELVIC INFLAMMATORY DISEASE caused by *N. gonorrhoeae*.

BACTERIAL SEPTICEMIA caused by *Staph. aureus*, *Strep. pneumoniae*, *E. coli*, *H. influenzae* and *K. pneumoniae*.

BONE AND JOINT INFECTIONS caused by *Staph. aureus*, *Strep. pneumoniae*, *Streptococcus* species (excluding enterococci), *E. coli*, *P. mirabilis*, *K. pneumoniae* and *Enterobacter* species.

INTRA-ABDOMINAL INFECTIONS caused by *E. coli* and *K. pneumoniae*.

MENINGITIS caused by *H. influenzae*, *N. meningitidis* and *Strep. pneumoniae*. Ceftriaxone has also been used successfully in a limited number of cases of meningitis and shunt infections caused by *Staph. epidermidis* and *E. coli*.

PROPHYLAXIS: The administration of a single dose of ceftriaxone preoperatively may reduce the incidence of postoperative infections in patients undergoing coronary artery bypass surgery.

Although ceftriaxone has been shown to have been as effective as cefazolin in the prevention of infection following coronary artery bypass surgery, no placebo-controlled trials have been conducted to evaluate any cephalosporin antibiotic in the prevention of infection following coronary artery bypass surgery.

SUSCEPTIBILITY TESTING: Before instituting treatment with Rocephin, appropriate specimens should be obtained for isolation of the causative organism and for determination of its susceptibility to the drug. Therapy may be instituted prior to obtaining results of susceptibility testing.

CONTRAINDICATIONS: Rocephin is contraindicated in patients with known allergy to the cephalosporin class of antibiotics.

WARNINGS: BEFORE THERAPY WITH ROCEPHIN IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS, PENICILLINS OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE THE USE OF SUBCUTANEOUS EPINEPHRINE AND OTHER EMERGENCY MEASURES.

Pseudomembranous colitis has been reported with the use of cephalosporins and other broad spectrum antibiotics; therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use.

ROCEPHIN® (ceftriaxone sodium/Roche)

Treatment with broad-spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis. Cholestyramine and colestipol resins have been shown to bind to the toxin *in vitro*.

Mild cases of colitis respond to drug discontinuance alone. Moderate to severe cases should be managed with fluid, electrolyte and protein supplementation as indicated.

When the colitis is not relieved by drug discontinuance or when it is severe, oral vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis produced by *C. difficile*. Other causes of colitis should also be considered.

PRECAUTIONS: GENERAL: Although transient elevations of BUN and serum creatinine have been observed at the recommended dosages, the nephrotoxic potential of Rocephin is similar to that of other cephalosporins.

Ceftriaxone is excreted via both biliary and renal excretion (see Clinical Pharmacology). Therefore, patients with renal failure normally require no adjustment in dosage when usual doses of Rocephin are administered, but concentrations of drug in the serum should be monitored periodically if evidence of accumulation exists; dosage should be decreased accordingly.

Dosage adjustments should not be necessary in patients with hepatic dysfunction, however, in patients with both hepatic dysfunction and significant renal disease, Rocephin dosage should not exceed 2 gm daily without close monitoring of serum concentrations.

Alterations in prothrombin times have occurred rarely in patients treated with Rocephin. Patients with impaired vitamin K synthesis or low vitamin K stores (e.g., chronic hepatic disease and malnutrition) may require monitoring of prothrombin time during Rocephin treatment. Vitamin K administration (10 mg weekly) may be necessary if the prothrombin time is prolonged before or during therapy.

Prolonged use of Rocephin may result in overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken. Rocephin should be prescribed with caution in individuals with a history of gastrointestinal disease, especially colitis.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY: Carcinogenesis: Considering the maximum duration of treatment and the class of the compound, carcinogenicity studies with ceftriaxone in animals have not been performed. The maximum duration of animal toxicity studies was six months. Mutagenesis: Genetic toxicology tests included the Ames test, a micronucleus test and a test for chromosomal aberrations in human lymphocytes cultured *in vitro* with ceftriaxone. Ceftriaxone showed no potential for mutagenic activity in these studies.

Impairment of Fertility: Ceftriaxone produced no impairment of fertility when given intravenously to rats at daily doses up to 586 mg/kg/day, approximately 20 times the recommended clinical dose of 2 gm/day.

PREGNANCY: Teratogenic Effects: Pregnancy Category B. Reproductive studies have been performed in mice and rats at doses up to 20 times the usual human dose and have no evidence of embryotoxicity, fetotoxicity or teratogenicity in primates, no embryotoxicity or teratogenicity was demonstrated at a dose approximately three times the human dose.

There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproductive studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nonteratogenic Effects: In rats, in the Segment I (fertility and general reproduction) and Segment III (perinatal and postnatal) studies with intravenously administered ceftriaxone, no adverse effects were noted on various reproductive parameters during gestation and lactation, including postnatal growth, functional behavior and reproductive ability of the offspring, at doses of 586 mg/kg/day or less.

NURSING MOTHERS: Low concentrations of ceftriaxone are excreted in human milk. Caution should be exercised when Rocephin is administered to a nursing woman.

PEDIATRIC USE: Safety and effectiveness of Rocephin in neonates, infants and children have been established for the dosages described in the Dosage and Administration section.

ADVERSE REACTIONS: Rocephin is generally well tolerated. In clinical trials, the following adverse reactions, which were considered to be related to Rocephin therapy or of uncertain etiology, were observed. **LOCAL REACTIONS**—pain, induration or tenderness at the site of injection (1%). Less frequently reported (less than 1%) was phlebitis after IV administration.

HYPERSENSITIVITY—rash (1%). Less frequently reported (less than 1%) were pruritus, fever or chills.

HEMATOLOGIC—eosinophilia (6%), thrombocytosis (51%) and leukopenia (21%). Less frequently reported (less than 1%) were anemia, neutropenia, lymphopenia, thrombocytopenia and prolongation of the prothrombin time.

GASTROINTESTINAL—diarrhea (27%). Less frequently reported (less than 1%) were nausea or vomiting, and dysgeusia.

HEPATIC—elevations of SGOT (31%) or SGPT (33%). Less frequently reported (less than 1%) were elevations of alkaline phosphatase and bilirubin.

RENAL—elevations of the BUN (12%). Less frequently reported (less than 1%) were elevations of creatinine and the presence of casts in the urine.

CENTRAL NERVOUS SYSTEM—headache or dizziness were reported occasionally (less than 1%).

GENITOURINARY—moniliasis or vaginitis were reported occasionally (less than 1%).

MISCELLANEOUS—diaphoresis and flushing were reported occasionally (less than 1%).

Other rarely observed adverse reactions (less than 0.1%) include leukocytosis, lymphocytosis, mono-cytosis, basophilia, a decrease in the prothrombin time, jaundice, glycosuria, hematuria, bronchospasm, serum sickness, abdominal pain, colitis, flatulence, dyspepsia, palpitations and epistaxis.

DOSEAGE AND ADMINISTRATION: Rocephin may be administered intravenously or intramuscularly. The usual adult daily dose is 1 to 2 gm given once a day (or in equally divided doses twice a day) depending on the type and severity of the infection. The total daily dose should not exceed 4 grams.

For the treatment of serious miscellaneous infections in children, other than meningitis, the recommended total daily dose is 50 to 75 mg/kg (not to exceed 2 grams) given in divided doses every 12 hours. Generally, Rocephin therapy should be continued for at least two days after the signs and symptoms of infection have disappeared. The usual duration is 4 to 14 days, in complicated infections longer therapy may be required.

In the treatment of meningitis, a daily dose of 100 mg/kg (not to exceed 4 grams), given in divided doses every 12 hours, should be administered with or without a loading dose of 75 mg/kg.

For the treatment of uncomplicated gonococcal infections, a single intramuscular dose of 250 mg is recommended.

For preoperative use (surgical prophylaxis), a single dose of 1 gm administered ½ to 2 hours before surgery is recommended.

When treating infections caused by *Streptococcus pyogenes*, therapy should be continued for at least ten days.

No dosage adjustment is necessary for patients with impairment of renal or hepatic function, however, blood levels should be monitored in patients with severe renal impairment (e.g., dialysis patients) and in patients with both renal and hepatic dysfunctions.

HOW SUPPLIED: Rocephin (ceftriaxone sodium/Roche) is supplied as a sterile crystalline powder in glass vials and piggyback bottles. The following packages are available:

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- Piggyback bottles containing 1 gm equivalent of ceftriaxone. Boxes of 10 (NDC 0004 1964 03)
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- Piggyback bottles containing 2 gm equivalent of ceftriaxone. Boxes of 10 (NDC 0004 1965 03)
- Bulk pharmacy containers, containing 10 gm equivalent of ceftriaxone. Boxes of 1 (NDC 0004 1971 01)

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* ROCEPHIN is indicated in the following infections: bacterial septicemia, bone and joint, intra-abdominal, lower respiratory tract, skin and skin structure, urinary tract, bacterial meningitis and gonorrhea. Please see summary of product information on adjacent page for indicated susceptible organisms.